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ORIGINAL ARTICLES

PRESIDENT'S ADDRESS

By WARREN W. QUILLIAN, M.D.
Coral Gables, Fla.

AN EXCELLENT opportunity has been afforded us during the past year to study carefully the record of Academy growth and development, the scope of its interests and activities, as outlined in that treasured volume, *The History of the American Academy of Pediatrics,* which was published and distributed during the past year. Dr. Marshall C. Pease has succeeded in presenting to the membership, in very entertaining fashion, a panorama of efforts made by us to understand and solve problems related to child health and welfare. For this labor of love and service, our Historian merits the sincere thanks of each member of the Academy. He has woven into the text very often bits of background and philosophy surrounding significant decisions which have affected our subsequent course. His energy, talent and hard work have resulted in a volume which reflects credit to the author and the organization about which he writes.

Consideration of the facts recorded in the written word of our history can give one little cause for worry concerning the sincerity, serious purpose, or idealistic concepts of those stalwart pediatricians who first proposed the organization of the American Academy of Pediatrics. Many of their dreams have not been fulfilled. Errors of judgment or of policy have, however, been honest; and, upon sober reflection, have often been corrected. The infant, born in 1930, now stands upon the threshold of maturity. His rapid physical growth and increasing influence among others having similar interests makes it imperative that he evaluate carefully the motivations, purposes and ideals which will determine his conduct.

The road ahead will have new horizons and different perspectives. This, then, might be termed the year of decision. He must clarify his objectives, and determine in what practical manner he can best measure up to his responsibilities; and justify the faith of his predecessors by meeting adequately the challenge of the future.

This is a good time to pause, and to take inventory of the efforts we are making to meet the demands of this changing era in pediatric practice. Vision is limited by the

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ability and perspective of the individual who makes the commentary. And the following thoughts are presented solely from the viewpoint of one whose sincere interest in the welfare of the Academy has never been questioned; but who, perhaps, is taking advantage of the prerogative which is traditionally accorded the President of the Academy, to indulge in an expression of his own philosophy and opinions concerning our affairs.

Occasional bewilderment and a need for orientation is inevitable in this rapidly changing world. This is true in our relationships with society, our responsibilities to others less fortunate, and our obligations to those who have preceded us. It is no less true within the framework of our own profession. The Study of Child Health Services and Pediatric Education revealed certain inadequacies in the complete care of the child in this country, despite the fact that American medicine represents achievement and accomplishment in this field exceeded by no other system of healing in the world. And pediatric progress has contributed much to these accomplishments during the past few decades.

Indeed, the National Board of Medical Examiners has recently recognized pediatrics as one of the four major classifications of medicine, ranking with surgery, internal medicine, obstetrics and gynecology. Every modern medical school now has a department of pediatrics. The American Board of Pediatrics, a portion of whose organization includes Academy representation, has kept high the standards for certification in our specialty.

During 1951 certain fundamental changes in organization of the Academy structure were effected, after many months of arduous effort. Increased duties and responsibilities delegated to the Executive Board emphasized again the importance of electing able and devoted representatives to this group.

Your present Board members have never faltered during this past year in an effort to fulfill their obligations to the membership; and their unselfish service has more than justified the confidence which you have placed in them.

There are a number of activities and programs based upon, and designed for, the practical realization of our long range objectives. Present emphasis is upon the problems of medical education, as the logical outgrowth of the needs disclosed by facts revealed in the Study of Child Health Services. The eventual goal, proper availability of the highest type of medical practice for the complete care of the child, is no small undertaking. Progress has not been gained by accident.

Committees

A great deal of productive work has been accomplished by our Committees. News-Letters and the official Academy publication, Pediatrics, have, throughout the year, kept our members informed concerning the activities of many of these. Those in attendance at this annual meeting will learn more about them at the various luncheons. Results attest the zeal and enthusiasm with which the Committee members have undertaken their tasks. The individual Academy member occasionally forgets how much so many of us owe to so few in the practical application of our ideals. It is desirable that we make plans to finance independently our Committee work so far as is possible. Accomplishment of our programs in the past would not have been possible without grants from commercial firms and financial aid from other sources. We are most grateful for this tangible evidence of approval from organizations and individuals interested in the work of the Academy.

Insurance Plans

In addition to the standing and scientific committees, which represent the life's blood of the Academy, during the year special groups have been designated to study insurance

plans, proposals for a life membership classification, and similar problems related to the interests of the Academy membership. Realistic consideration of recent trends in medicine necessarily includes the rapidly growing medical care plans which are developing throughout this country and Canada. It is very proper for us to become acquainted with the details, methods of administration and comparative advantages of the various proposed programs. Voluntary health insurance constitutes one of the constructive answers to recent agitation concerning a National Compulsory Health program. Our patients have a right to expect of us a reasonable familiarity with the practical application of these insurance plans; and to warn them concerning pitfalls which lurk in the fine print on the policy. Too often the economic shock of prolonged, serious illness places a strain upon the financial reserve of families. It is logical to assume that better medical care can most efficiently be administered in a system of free enterprise and in accordance with traditions of our American way of life. An alternative plan has been proposed by those who advocate government operated medical care; and who desire legislation to make of this program the law of the land. The latter has been described as the "allotment of an unknown sum for an unpredictable purpose." An objective, unbiased evaluation of the various plans for voluntary medical care insurance, and for different methods of providing service, has been made during the past year by the committee of which Dr. Edward A. Wishropp is Chairman.

Another special committee, under the leadership of Dr. Archibald L. Hoyne, is investigating, and will make recommendations concerning, proposals for affording group health and accident insurance to the membership of the Academy.

Liaison

Expanding application of efforts to help other organizations interested in allied fields of activity is apparent. Our liaison is far reaching. Academy objectives and purposes are thus placed on a practical basis. Leadership involves responsibility and obligation to others. It must be pointed out, however, that we can easily dilute our effectiveness by spreading too thin; and by making too diversified our efforts to help other groups. The time has come to strengthen old ties, and to measure the value of our relationships by the standard of their eventual effect upon the welfare of children.

District IX

Good will among Latin American pediatricians seems to have been enhanced by our official representation at the Pan American Congress of Pediatrics in Montevideo (December 1951). About 16 Academy members from the United States attended. More effective cooperation with District IX is reflected in extension of services, which include translation of publications into the Spanish language, in help with the planning and financing of the Pan American Congresses, and in offering encouragement for more active participation in Academy affairs.

State Chairmen

The organizational meeting of State Chairmen held here this week is an attempt to correlate and crystallize the opinions of 61 different zones in the Academy.

There is an opportunity for this group to be a source of great strength in the formulation of policy and the successful solution of problems which will confront us in the years to come. Underlying all else is the universal desire to elicit the interest and participation

of our membership at large. Specific programs for betterment of child health must be carried out with the aid of individual Academy members as they function through existing medical groups in the states and countries of our organization. Individual states must plan projects appropriate to their needs, as determined by an active, interested membership.

Expanding Services

Growth of the Academy to its present maturity has been characterized by a solid foundation of achievement. It is not possible to describe here in detail many of the complex activities of an organization now composed of more than 3,400 members. Demands of a growing membership have necessitated changes in structure, increased administrative personnel and more adequate quarters for the Central office. Re-organization in 1951 provided the facilities and equipment for greater efforts on a constructive basis. During April 1952 the Central office was moved to 610 Church Street, Evanston, Illinois. The new lease for five years provides more space for our administrative personnel at a substantial saving. The move reveals the business acumen and keen foresight of our Executive Secretary. A growing membership and expanding services have emphasized the need of a permanent home for the Academy. Your Executive Board, in May (1952), created a Building Fund, with the idea of studying plans for the accomplishment of this purpose.

Certain changes in the By-laws will be recommended at this meeting. These modifications are based upon a desire within the Executive Board to give to the individual member more freedom and voice in Academy affairs.

Economy and efficiency of operation are reflected in the reports of the Treasurer and the Executive Secretary. Dissemination of knowledge has kept pace through the medium of our scientific meetings, seminars and round table discussions.

The well earned position which PEDIATRICS holds in the field of publications is a source of pride to every Academy member. According to actuarial statistics, an infant born in 1952 has a 20% greater chance of reaching maturity, and a 44% greater likelihood of surviving to the age of 50, than a baby born in 1900. During this same period, 20 years have been added to the life span of the American people. These facts reflect favorably the quality of medical care administered by graduates of medical schools privileged to practice in an atmosphere of individual and scientific freedom. Medical progress has been phenomenal. Introduction of modern drugs, and methods of immunization and widespread use of weapons added to our therapeutic armamentarium, have changed the whole character of pediatric practice. Shifting emphases have brought into focus the problems of growth and development in the well child. Happily, despite these changes, there has been no alteration of the ideals and aims which are basic to the practice of our profession.

Members

The esteem with which the Academy is held as an organization is determined by the character and life of the individual member. Our course has been indelibly associated with the attitudes and abilities of individuals. We have a glorious heritage and a tremendous new responsibility for the health and welfare of children. Are we keeping the faith? Leadership must be provided in our home communities.

The "Principles of Ethics" of the American Medical Association states that the "prime object of the medical profession is to render service to humanity; reward or financial gain is a subordinate consideration." Application of this broad principle to our daily lives and practice requires conscientious devotion to ideals as well as the use of the skills we possess.

It is fundamental that our talents must be utilized in helping others. The pediatrician must not shirk his responsibility in the realm of spiritual values. Personal integrity and moral responsibility are attributes which the patient has a right to expect in his personal physician. Honesty and an humble spirit are qualifications which must be rated as important as training, experience and intelligence.

Public Relations

One of the obvious problems in practice is the betterment of our public relations. More time must be spent in giving to the public actual facts concerning medical care and in cooperation with lay groups whose activities influence public opinion. The help of every member of the Academy is needed in his home community for intelligent planning and for progress in the solution of this problem. Active interest of the pediatrician in the social problems of the community is imperative, if our goals are to be reached. Public health, facilities for the care of the handicapped, environmental factors predisposing to juvenile delinquency, and health education are all a part of his concern and responsibility. The greatest force in our field of public relations is the individual pediatrician at his daily task.

Community Responsibility

The American citizen is becoming awakened to a serious lack of moral responsibility in public life. Vaguely, he feels that this may be his own fault. Within a few weeks American voters will have the privilege of casting ballots in the presidential election. According to Senator Owen Brewster (Maine), if the same number of persons fail to vote this year as in the last presidential election, approximately 48 million Americans will forfeit the privilege of having a part in selecting our leader for the next four years. Surely it is a responsibility of the Academy member as a citizen to exert his influence locally by precept and example, in this connection.

Support of sound health education programs in the schools and speeches on medical subjects before civic organizations will inevitably lead to better relations with the citizens whose interests we serve. Tact and skill are required of the physician in his contacts with the parents as counselor concerning such important daily relationships as the selection of nursery schools, methods of spending recreation time, proper school placement and the correction of faulty environmental factors. Radio programs and movies have great public appeal; and they exert a tremendous effect upon the thinking and behavior of young America. Yet there is no widespread or concerted effort by the medical profession to assist broadcasters or motion picture producers in the selection of proper material for presentation. Here is an opportunity for the pediatrician, as a leader in community life, to influence public opinion; and to render a real service toward the improvement of general standards of entertainment.

Conclusion

Economic and social progress in our practice depends upon the sustained interest and the effort of the individual physician. Courage and faith are necessary foundations for action in this critical year of decision, and there is every reason to believe that the new generation of pediatricians has every qualification necessary to continue the quest for better health among children. His adventure in "practical idealism" will not be an easy one. But, fortified by the assurance of his noble heritage of accomplishment and adherence to high standards, he will accept the challenge of the future with a deep sense of responsi-

bility. He will keep faith with those who have gone before, and attempt to retain the confidence and trust of the people as did our fathers, by holding high the banner of service.

The price of success in this undertaking involves a determination to reach our objectives regardless of adverse circumstances, concentration on the immediate problems, and by long range plans for fulfilling our obligations to the children of America. Frustration and differences of opinion are inevitable. Changing conditions require flexibility in our adaptation to existing needs. Let us keep our eyes upon the stars, but our feet upon the ground! Our responsibilities are great. The Dean of the School of Medicine at the University of Wisconsin, Dr. William S. Middleton, recently stated the challenge in these words: "Make no small plans; they have no magic to stir man's soul!"

Medicine progresses, even in a troubled world. Changes in governments, in laws and controls, have not interfered with this progress. Civilizations of the past have been destroyed by the decay and infamy and greed within their own structure. Let us renew our faith in the simple basic principles, which have characterized the growth and development of the Academy for 22 years.

140 Alhambra Circle

COMPARATIVE EFFECTS OF PENICILLIN, AUREOMYCIN AND TERRAMYCIN ON STREPTOCOCCAL TONSILLITIS AND PHARYNGITIS

By FLOYD W. DENNY, M.D.,* LEWIS W. WANNAMAKER, CAPT., MC, USAR,* AND EDWARD O. HAHN, MAJ., MC, USAR
Cleveland

THE variety of antibiotics now available to the practicing physician has complicated rather than simplified the problem of selection of the most effective drug for the treatment of specific infections. Although results from *in vitro* studies and from therapy of experimental infections assist in the selection of the most efficacious drug, final evaluation must be made by comparative observations in man. The present study is a clinical evaluation of the relative merits of penicillin, aureomycin and terramycin for the treatment of group A streptococcal tonsillitis and pharyngitis.

DESCRIPTION OF THE STUDY

This study was conducted at Warren Air Force Base, Wyo., between March 31 and May 4, 1951. A homogeneous group of early streptococcal infections was selected by the following criteria:

TABLE 1

COMPARABILITY OF TREATED AND CONTROL GROUPS

	Treatment Group			
	Control (50 cases) %	Penicillin (53 cases) %	Aureomycin (53 cases) %	Terramycin (51 cases) %
History of tonsillectomy	36	23	49	33
Age 17–21 yr.	84	91	83	92
Group A streptococci on admission culture	98	91	96	96
Type 1	14	17	17	33
Type 5	10	9	13	4
Type 6	8	8	8	10
Type 14	46	47	53	43

(1) exudate on the tonsils or pharynx, (2) a total leucocyte count of 10,000 or greater and (3) duration of symptoms less than 31 hr. Patients were assigned to 1 of 4 therapeutic groups according to corresponding suits in decks of well shuffled cards. Fifty-three patients were treated with peni-

From the Streptococcal Disease Laboratory, Francis E. Warren Air Force Base, Wyo., and the Department of Preventive Medicine, Western Reserve University, School of Medicine, Cleveland.

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* Present address: Heart Hospital, University of Minnesota Medical School, Minneapolis.

cillin, 53 with aureomycin, 51 with terramycin and 50 received placebos. The 4 groups of patients appeared to be comparable (table 1) except for an unexplained variation in the number of patients giving a history of tonsillectomy. Approximately one third of all patients gave such a history, but the percentage ranged from 23 in the penicillin group to 49 in the aureomycin group.

Penicillin was administered by intramuscular injection of 600,000 units of crystalline procaine penicillin G* daily for 5 days. Crystalline aureomycin hydrochloride* or crystalline terramycin hydrochloride* was given orally in a dose of 1 gm. on admission and 0.5 gm. every 6 hr. for 19 additional doses. The control patients received lactose placebos every 6 hr. for 20 doses. No other medication was allowed except codeine for severe discomfort.

All patients were questioned and examined daily for 6 days by 2 physicians who had no knowledge of the treatment being administered. Symptoms were recorded for each 12 hr. period for the 1st 48 hr., and daily thereafter. Physical signs were recorded daily. Oral temperatures were recorded every 4 hr. Total leucocyte counts were determined on the 1st 3 days of hospitalization. Cultures were obtained from the oropharynx on the 1st, 2nd, 3rd and 5th days of hospitalization and on approximately the 21st day after the onset of illness at the time of follow-up examination. Acute phase sera were obtained on the 1st or 2nd day of illness and convalescent phase sera at the time of the follow-up examination. Electrocardiograms consisting of the 3 standard limb leads were recorded within several days after admission, and again on the 6th, 8th, 10th, 14th and 21st days of illness. The patients were questioned at these times for the presence of complications.

Strains of Str. beta hemolyticus were grouped and typed according to the method of Swift, Wilson and Lancefield.[1] Antistreptolysin "O" titers were determined by a modification of the method of Hodge and Swift.[2]

Results

The effect of treatment on the symptoms of streptococcal sore throat is demonstrated in chart 1. Treatment with penicillin, aureomycin or terramycin reduced the number of patients who complained of headache and sore throat. Aureomycin tended to be less effective than the other two drugs in reducing the prevalence of headache. The effect of treatment on sore throat was approximately the same in all groups. In general, patients without tonsils complained of less sore throat than did those patients who had tonsils. Because of the high percentage of tonsillectomized patients in the aureomycin group the demonstrated effect of treatment with this drug may be exaggerated. With the symptom chilliness there was little or no difference noted among any of the groups. The incidence of anorexia and nausea in the patients receiving aureomycin was equal to that observed in the control group. Sixteen per cent of the patients in the control group vomited at some time during the clinical course, but the incidence was 29% in the aureomycin group and only 9 and 8% in the penicillin and terramycin groups, respectively. Aureomycin and terramycin produced more diarrhea than did either penicillin or the placebo. Forty-five per cent of the patients in the former two groups gave a history of loose stools on the fourth day of illness.

The effect of treatment on the physical signs of streptococcal sore throat is shown in chart 1. The three forms of treatment were approximately equal with respect to their effect on the manifestations of inflammation except that the disappearance of exudate was somewhat less rapid in the patients treated with penicillin than in the other two treated groups. In the penicillin group a low percentage (23%) of patients and in the aureomycin group a high percentage (49%) of patients had had their tonsils removed. Since tonsillectomized patients lost their exudate more rapidly than did those with tonsils, the effect of penicillin on the disappearance of exudate may be unduly minimized and the effect of aureomycin may be magnified.

* Penicillin (duracillin) was supplied by Eli Lilly and Company, Indianapolis; aureomycin hydrochloride by Lederle Laboratories Division, American Cyanamid Company, New York, and terramycin hydrochloride by Charles Pfizer and Company, New York.

The per cent of patients in each group who had fever of 37.8°C. or over for each four hour period is shown in chart 2. All three forms of therapy were effective in reducing fever, and there is little difference in the rate of defervescence among the treated groups.

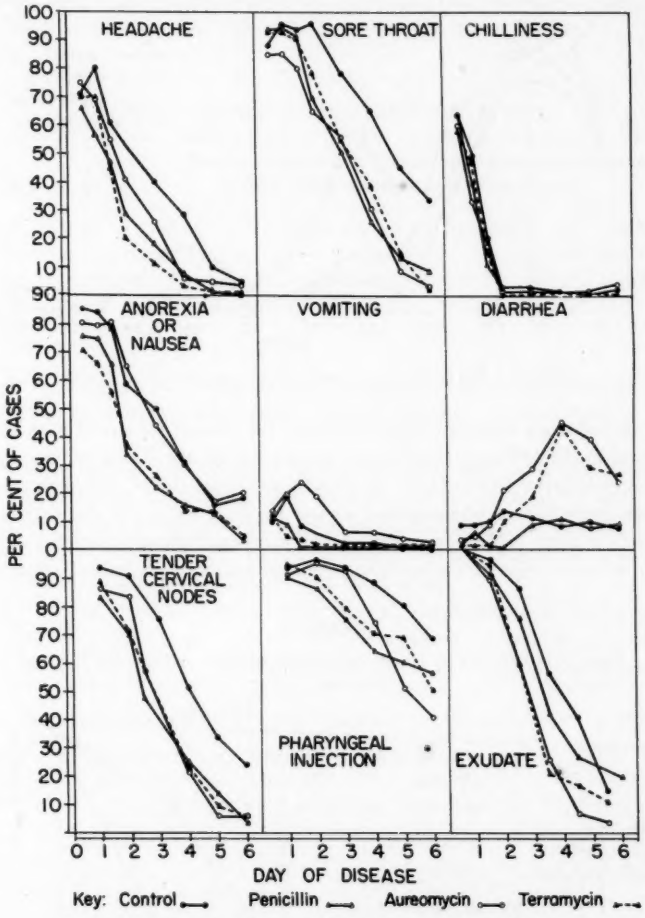

CHART 1. Effect of various antibiotics on symptoms and signs of acute streptococcal tonsillitis and pharyngitis.

When all groups were considered together, a history of tonsillectomy seemed to have no effect on the disappearance of fever.

Suppurative complications occurring within 14 days after the onset of the acute illness were rare in all the groups (table 2). Only those complications appearing after therapy had been instituted for at least 24 hours are included. The same type of group A streptococcus was identified at the time of both illnesses except for three patients in the terramycin group from whom a different type group A streptococcus was isolated at the second illness, and one patient in the aureomycin group who harbored Str. beta hemolyticus of unidentified type at the time of the second illness.

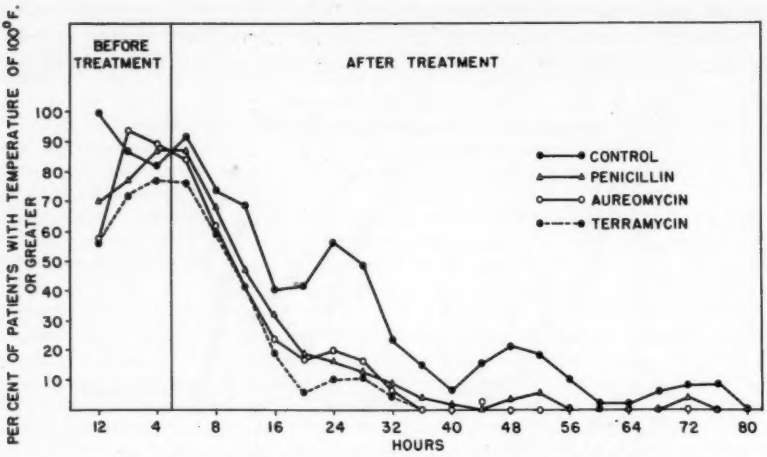

CHART 2. Effect of various antibiotics on occurrence of fever.

Three cases of acute rheumatic fever followed the illnesses observed in this study. One each occurred in the control, penicillin and terramycin groups. These began 31, 27 and 19 days, respectively, after the onset of the streptococcal sore throat. No history of an intervening respiratory illness was obtained in any of these men, but the patient from the control group and the patient from the penicillin group showed bacteriologic evidence of acquisition of a new type of streptococcus. In addition, both the patient from the control

TABLE 2

EFFECT OF THERAPY ON COMPLICATIONS OF STREPTOCOCCAL SORE THROAT

Complication	Treatment			
	Control (50 cases)	Penicillin (53 cases)	Aureomycin (53 cases)	Terramycin (51 cases)
Suppurative:				
Exudative tonsillitis	1	1	1	3
Peritonsillar cellulitis	0	0	0	1
Sinusitis	1	0	0	0
Ear ache	2	0	0	0
Nonsuppurative:				
Rheumatic fever	1	1	0	1
PR>0.21 sec.	0	0	0	1
T_1 inverted or flat	0	0	0	0
No rheumatic fever	49	52	53	50
PR>0.21 sec.	0	1	0	1
T_1 inverted or flat	1*	0	1†	1

* This patient also had a sedimentation rate of 20 (Wintrobe method) and maximum observed temperature of 40.0° C.

† This patient also had aching and tenderness of R knee for 3 days, maximum sedimentation rate of 23 (Wintrobe method) and maximum observed temperature of 40.0° C.

group and the patient who received terramycin gave a questionable past history of rheumatic fever.

Abnormalities of the electrocardiogram are shown in table 2. They were rare in all groups. Three patients, one from the penicillin group and two from the terramycin group, had a prolonged conduction time. One of the latter had concomitant manifestations of

TABLE 3

EFFECT OF THERAPY ON TOTAL LEUCOCYTE COUNT

Hospital day	Per cent of patients with total leucocyte count greater than 10,000 according to treatment group			
	Control	Penicillin	Aureomycin	Terramycin
First	96	100	98	98
Second	96	87	85	76
Third	52	42	19	14

rheumatic fever. Three patients showed T-wave changes in lead one. There was one each from the control, aureomycin and terramycin groups, none of whom developed rheumatic fever.

Total leucocyte counts were obtained on the first three days of hospitalization on all patients. The percentage of counts greater than 10,000 is presented by hospital day in table 3. All the treated groups showed a decrease on the second day as compared to the control group. On the third day the decline in leucocytosis was more striking in the aureomycin and terramycin groups than in the penicillin group.

The effect of treatment on the infecting type of streptococcus is shown in chart 3. Only those patients from whom a group A streptococcus was isolated at some time during hospitalization are included. By the fifth day of illness all forms of therapy had greatly

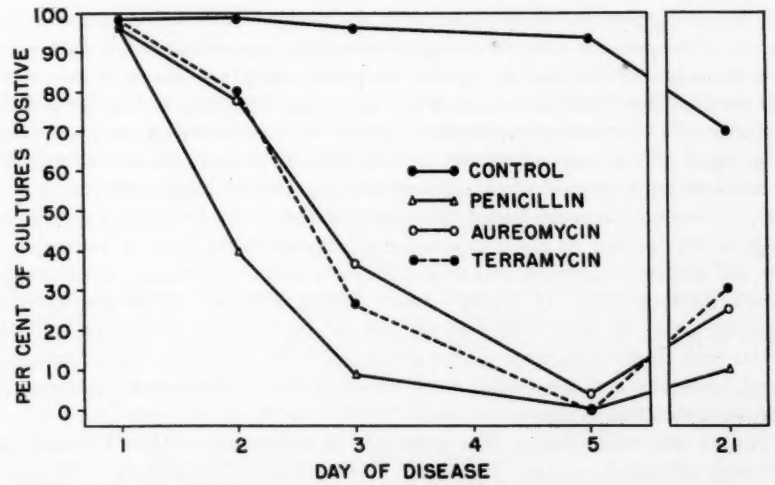

CHART 3. Effect of various antibiotics on persistence of infecting type of streptococcus.

reduced the carrier rates, while the rate in the control group was still very high. Penicillin resulted in a more rapid reduction in the carrier rate than did either aureomycin or terramycin. Likewise at the time of the follow-up examination 21 to 33 days after the onset of the acute illness, the carrier rate for the group treated with penicillin was lower than that for either the aureomycin or terramycin groups. The percentage of cases in which a new type of streptococcus was isolated at follow-up was 11 in the control group, 14 in the penicillin group, 8 in the aureomycin group and 9 in the terramycin group.

Table 4 shows the effect of treatment on the development of antistreptolysin O. Although there was some variation in the average titer of the acute phase sera, therapy with

TABLE 4

EFFECT OF THERAPY ON ANTISTREPTOLYSIN O PRODUCTION

	Average titer (in units) according to treatment group			
	Control	Penicillin	Aureomycin	Terramycin
Acute	124	110	116	144
Convalescent	294	196	188	213
Difference	170	86	72	69
Per cent reduction	—	49	58	59

each drug resulted in decreased antibody formation. The per cent reduction was 58 for aureomycin, 59 for terramycin and 49 for penicillin.

DISCUSSION

A beneficial therapeutic effect was demonstrated in patients with streptococcal tonsillitis and pharyngitis following administration of penicillin, aureomycin or terramycin. No one drug was consistently more effective than the other two. This is in contrast to a study reported previously[3] where aureomycin was more effective than penicillin in these respects. In the previous study the dosage of aureomycin administered during the first 24 hours was 4 gm. as compared to 3 gm. in the present study. Conversely, in the previous study the penicillin dosage during the first 24 hours was 300,000 units of depot penicillin containing 2% aluminum monostearate in peanut oil whereas during the present study this group of patients received 600,000 units of procaine penicillin on the first day. Since the effect on fever, physical signs and symptoms can best be demonstrated early in the course of treatment, it seems logical that these differences may be due to a difference in dosage during the first 24 hours. A possible explanation of the effect of aureomycin on fever and associated symptoms may be an antipyretic action.[4] This might be more apparent with the larger dose. There was a rather striking difference in the gastrointestinal complaints among the three treated groups. The incidence of anorexia, nausea and vomiting was high in the aureomycin-treated group and both aureomycin and terramycin increased the incidence of loose stools. From the standpoint of toxicity it would appear that penicillin is the drug of choice.

Penicillin was more effective than terramycin or aureomycin in short and long term eradication of streptococci from the throat. This is in agreement with previous studies[3] except that the present dose of 10.5 gm. of aureomycin over a five day period appeared

to be considerably more effective in eradicating streptococci than the previous dose of 8.5 gm. over a four day period where no effect was demonstrable at 21 days.

All three forms of therapy resulted in a decrease in antibody formation. Leucocyte counts returned to normal more rapidly in the terramycin and aureomycin groups than in the penicillin group. These data are in agreement with previous observations on penicillin and aureomycin.[3]

Since, except for toxicity, there was little difference among the three groups in the acute course of the disease, the choice of drug should probably be made on the basis of eradication of the carrier state and the effect on suppurative and nonsuppurative complications. The incidence of recurrent exudative tonsillitis was slightly higher in the terramycin group but in other respects the suppurative complications were equal in the three treated groups. The incidence of rheumatic fever was too low in this study to evaluate the effect of these drugs but results of other studies[5] seem to indicate that penicillin may be slightly more effective than aureomycin in this regard. No study has been reported on the effect of terramycin in prevention of rheumatic fever.

Summary

The effects of penicillin, aureomycin and terramycin on the clinical course of streptococcal tonsillitis and pharyngitis were compared in a controlled study. Under therapy with these agents most of the symptoms and signs subsided somewhat more rapidly than in control patients, leucocytosis was reduced and antibody formation was diminished; but in the dosage used no one drug was consistently most beneficial. Penicillin was the most effective drug in eradicating streptococci from the throat. Nausea and vomiting occurred frequently among the patients receiving aureomycin, and diarrhea was common in both the aureomycin and terramycin treated groups. Final determination of the drug of choice should await comparison of the effects on suppurative and nonsuppurative complications in larger groups of patients.

Acknowledgments

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SPANISH ABSTRACT

Efectos Comparativos de la Penicilina, Aureomicina y Terramicina en las Amigdalitis y Faringitis Estreptocócicas

En vista de la variedad de antibióticos disponibles, la selección del más efectivo de ellos para el tratamiento de infecciones específicas, se ha complicado, mas bien que simplificado y como la evaluación final debe hacerse por observaciones comparativas en el hombre, los autores hicieron este cuidadoso estudio. Trataron 53 enfermos con penicilina, otros tantos con aureomicina, y 55 con terramicina que representaban un grupo homogéneo de infecciones estreptocócicas tempranas siguiendo el criterio siguiente: exudado faringeo o amigdalino, leucocitosis de 10.000 o mayor y duración de los síntomas de menos de 31 horas. El grupo se comparó con 50 enfermos que recibieron placebos. Se usó penicilina procaína cristalina G a la dosis de 600.000 unidades diarias por 5 días y 1 gramo de aureomicina o terramicina como primera dosis y después ½ gramo cada 6 horas dándose 19 dosis adicionales.

Los resultados demuestran que los tres antibióticos produjeron efectos terapéuticos benéficos pero ninguna droga fué mas efectiva que la otra. La mayor parte de los síntomas y signos desaparecieron algo mas rápidamente que en el grupo control.

Es posible que la mayor eficacia que se adjudicó la aureomicina en un estudio previo se explique por diferencias de dosificación usada en las primeras 24 horas durante las cuales el efecto sobre la fiebre, signos físicos y síntomas puede ser mejor demostrado.

La penicilina fué mas efectiva en la erradicación, a corto y largo plazo, de los estreptococos de la faringe.

Los tres antibióticos produjeron una disminución en la formación de anticuerpos. La leucocitosis descendió a lo normal mas rápidamente en los grupos tratados con aureo y terramicina.

Se presentaron nauseas y vómitos mas frecuentemente con la aureomicina y fué común la diarrea con ésta y la terramicina.

La determinación final de la droga de elección debe regirla la comparación de su eficacia en la prevención de complicaciones en un grupo mas grande de enfermos.

Western Reserve University

COMPARATIVE STUDY OF CANINE DISTEMPER AND A RESPIRATORY DISEASE OF MAN

By JOHN M. ADAMS, M.D.
Los Angeles

A NEW form of epidemic pulmonary disease was described in 1941, occurring in prematurely born and young infants.[1,2] A uniform clinical pattern which varied in severity from mild cough and sneezing to severe cough, dyspnea, cyanosis and death was observed in all the patients in the epidemic. A biphasic temperature curve was reported. The disease was highly contagious, particularly in the infant wards of the institutions where it was first studied. Distinctive pathologic lesions with proliferation and destruction of pulmonary lining epithelium, a predominant mononuclear exudate and characteristic inclusion bodies were described for the first time in humans in connection with an epidemic pulmonary disease.

This syndrome has been observed sporadically and there is now increasing evidence that it may occur not infrequently in human beings in mild or inapparent form.[3] A striking difference in the morbidity and mortality was shown between full term infants and prematures.[4] The prematurely born infants, who are probably the most susceptible human hosts, were the most severely ill; mild and inapparent infection occurred in older infants and children.

It is the purpose of this paper to report experimental evidence of a relationship between the above human respiratory disease and canine distemper, which is the commonest known respiratory disease of dogs.

The author has shown a complete neutralization of the distemper viral infection in living chick-embryos by means of human sera and human gamma globulin. The experimental infection in young ferrets has been neutralized by gamma globulin of human source in both in vitro and in vivo experiments.

A comparative pathologic study of canine distemper in animals and humans will be presented briefly with the aid of photomicrographs. In the section on historical data, the epidemiologic and clinical similarities between common human respiratory disease and canine distemper will be outlined as revealed by a review of the literature.

HISTORICAL DATA

As early as 1809, Jenner gave an accurate description of distemper as it occurred in fox-hounds and drew a comparison with the infectious fevers of man. Distemper has been known to occur in the canine population of most countries of the world for many years and various bacteria were held responsible for its etiology until fairly recent times. In 1905, Carré[5] first presented evidence of transmission by means of bacteria-free filtrates.

From the Pediatric Department of the University of California, School of Medicine, Los Angeles; the University of Minnesota Medical School, Minneapolis, and the Veterans Administration Hospital, Long Beach, Calif.

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B. bronchisepticus was found constantly, however, by many investigators and it was not until the reports of the scientific committee of the Field Distemper Council were completed (1926) that the controversy was settled in favor of the original work of Carré. B. bronchisepticus, as well as other organisms, were established as secondary infectious agents.

Laidlaw and Dunkin[6] demonstrated first that six different strains of distemper caused one type of disease in ferrets and that "these strains cross-immunized against each other." They concluded that distemper is a single entity and that the response of the ferret to infection is comparable in all essentials with that of the dog; that distemper can be transmitted by filter-passing material which yields no growth in ordinary culture media and therefore "belongs to the class of filter-passing viruses."

Nicollé[7] reported experimental evidence of a relationship of distemper to an infection in man. He records the successful transmission of distemper to man in an inapparent form. In these experiments man, monkeys and dogs were inoculated at the same time with a known strain of distemper virus. When the disease was at its height in the experimental dogs, he was able to transmit it to other normal puppies by means of blood taken from the human host. He interprets this finding as evidence of an inapparent infection in man and states that man can serve as a reservoir of virus for animals or vice versa. He comments further that if two species are susceptible to a viral infection, and in one it is obvious, in the other subclinical, then the disease is older in the second species; he reasons that therefore distemper is an original disease of man. Nicollé states that its expression may have disappeared from man due to transmitted immunity but, when passed to dogs, appears as a clinical disease. He was concerned with adult human beings as subjects and may not have fully recognized the signs of infection in human beings at different age levels, such as premature and young infants and older susceptible individuals.

Bryan[8] reports observations on the transmission of a respiratory disease from himself to four puppies; all four within 7 to 10 days "went down with the typical picture of canine distemper." He reports also that while serving as veterinarian to a kennel club dog show he suffered from a severe case of "la grippe" following each show. Four additional cases involving 11 children are reported in his paper, all presenting evidence of a relationship between proved distemper and human respiratory tract infections.

Whitney[9] states that "housedog disease" is pharyngo-laryngo-tracheitis, and "that dogs can contract it from people who are suffering with a definite kind of cold." He believes this disease, although frequently confused with distemper, is a different entity caused by another virus.

Animals and birds are known to be a reservoir of human infectious diseases.[10] Relationships are known to exist between human and swine influenza, ornithosis of man and birds, small pox and cow pox, Q fever of humans and a bovine disease caused by the same rickettsial organism. The systemic form of distemper causes a febrile illness with respiratory symptoms predominating. Encephalitis is frequently associated with distemper in puppies in about 5% of the cases. Vuori[11] observed a 21 year old patient with transient paralysis of the facial muscles, diplopia and nystagmus, a stiff neck, hyperesthesia and exaggerated reflexes which developed three weeks after intimate contact with a dog with distemper. The author suspected the illness might have been related to the distemper of the dog.

Distemper is described as a highly infectious disease, having a characteristic biphasic

temperature curve. Dogs survive the disease but it may have a high fatality rate in young dogs during epidemics. At times the clinical picture in dogs is complicated by neurologic symptoms. There may be hardening of the foot pads, called "Hard Pad Disease." The disease produces a characteristic pathologic picture. Antigenically, there appears to be a cross-immunity between these diseases. Ferrets may die of a disease clinically and pathologically indistinguishable from distemper on transmission of virus.

Comparative Pathologic Studies

The most outstanding and constant clinical pathologic finding in distemper is the presence of inclusion bodies in the lung sections. They may be found in the urinary sediment cells and in bladder sections.

De Monbreun[12] describes an interstitial pneumonia with peribronchial involvement made up of infiltrated mononuclear cells and destruction of the lining epithelium as the most prominent finding. His description of the inclusion bodies in the dog's lung is as follows: "In all cases cytoplasmic inclusions were found in both bronchial and alveolar epithelial cells. In some bronchi these were especially abundant. They were situated in definite vacuoles and appeared well defined, usually round to oval, sometimes elongated, vacuolated acidophilic bodies most often lying between the nucleus and the outer margin of the cell, but sometimes at the opposite poles of the cell."

This paper has described pathologic lesions in human premature and full term infants which are comparable to those seen in sections from dogs and ferrets dying of proved distemper.[2-4] The lining epithelial cells of the respiratory passages contain similar cytoplasmic inclusion bodies and cellular changes. Proliferation with giant cell formation has been observed also in human lung sections (see Fig. 1). The staining characteristics using many different stains appear to be identical.

Identically appearing inclusion bodies have been found in bladder sections from dogs with distemper and in human urinary tract lining cells. Emphasis should be given to the size, shape and position of these bodies. The same vacuolation is seen in the inclusions of both man and animals (see Figs. 2-4).

The pharyngeal lining epithelium of human beings obtained from swabbings of the posterior pharynx have been found to show inclusion bodies in the epithelial cells in varying numbers, particularly in association with mild respiratory inflammations and throat irritations of one kind or another. The cell inclusions by various stains are identical morphologically with those seen in the trachea-lining cells and in the bronchial- and bronchiolar-lining epithelium of human beings. They also compare with the inclusion bodies seen in the pharyngeal epithelium of monkeys following inoculation with human washings[13] and appear to be identical to the bodies seen in the epithelial tissues throughout the respiratory tree of dogs and ferrets with proved distemper. (Fig. 1-6.)

Neutralization Studies

Studies were designed to test human serum and human gamma globulin compared with hyperimmune distemper antiserum and ferret immune serum. Ferrets and chick embryos were employed. Appropriate controls were followed in each experiment. Dog and ferret spleen virus, distemperoid virus and chick embryo-adapted virus (Lederle) were used in various doses.*

* A few of the neutralization tests in the chick embryos were done by the Lederle Laboratories through the kindness of Drs. Herald Cox and Victor Cabasso.

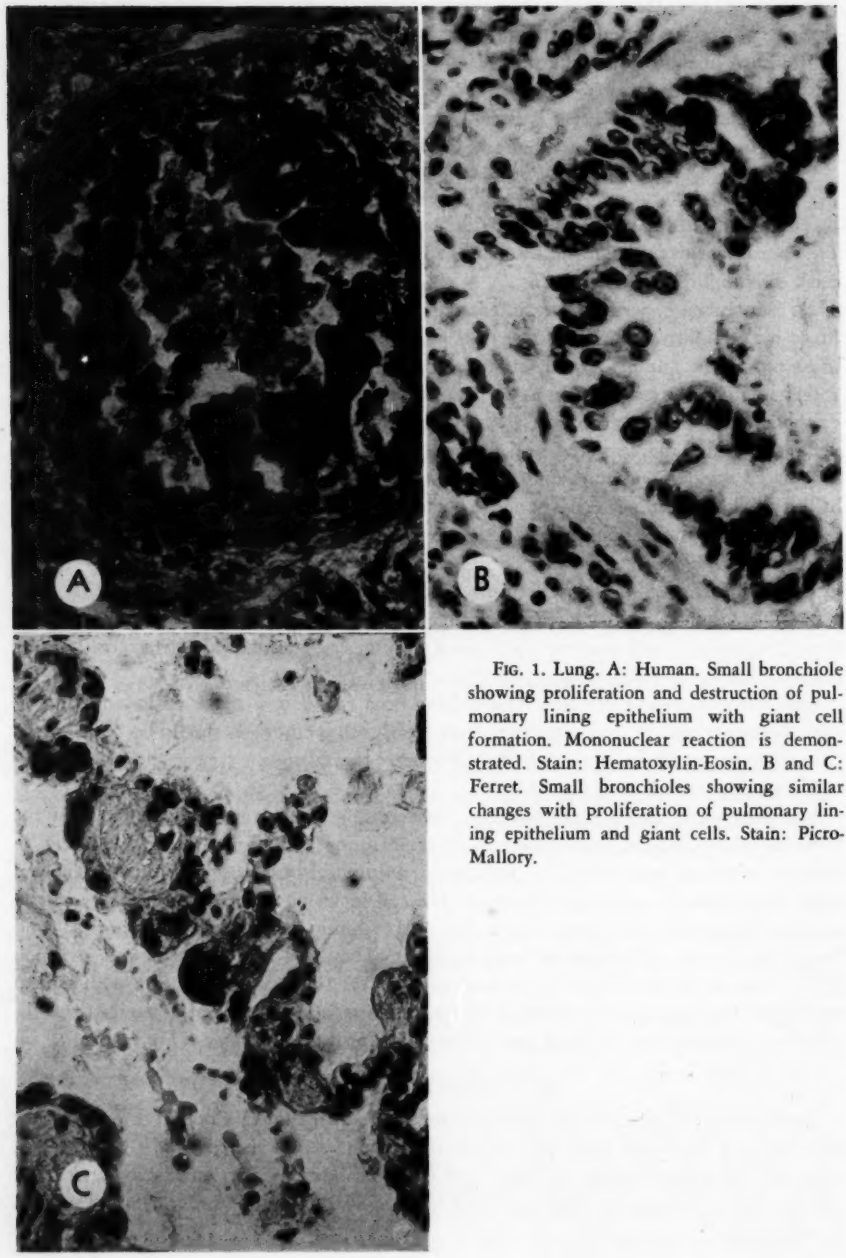

FIG. 1. Lung. A: Human. Small bronchiole showing proliferation and destruction of pulmonary lining epithelium with giant cell formation. Mononuclear reaction is demonstrated. Stain: Hematoxylin-Eosin. B and C: Ferret. Small bronchioles showing similar changes with proliferation of pulmonary lining epithelium and giant cells. Stain: Picro-Mallory.

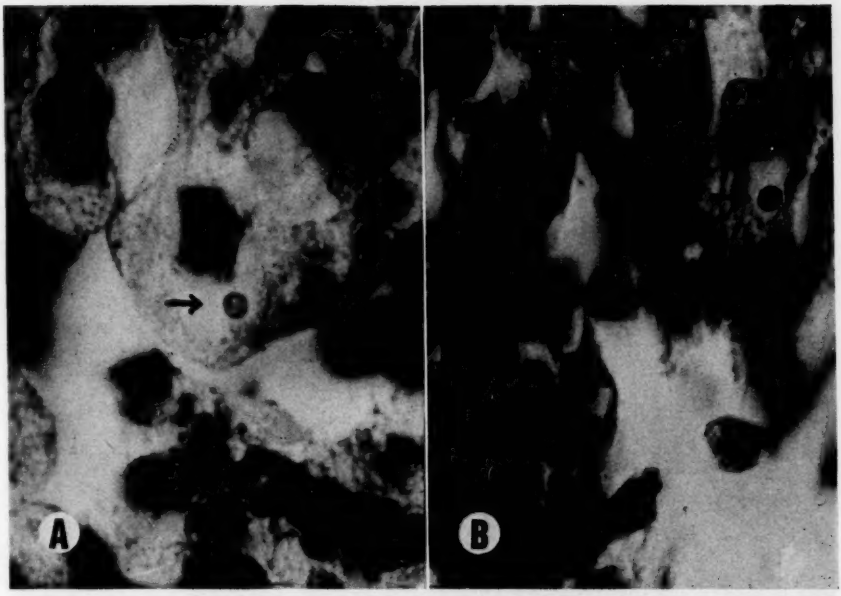

FIG. 2. Lung. A: Human. Swollen pulmonary epithelial cell with inclusion body in cytoplasm. Note vacuolation about inclusion and also evidence of vacuoles in body itself. Stain: Hematoxylin-Eosin. B: Dog. Pulmonary epithelial lining cells with cytoplasmic inclusion bodies. Stain: Hematoxylin-Eosin.

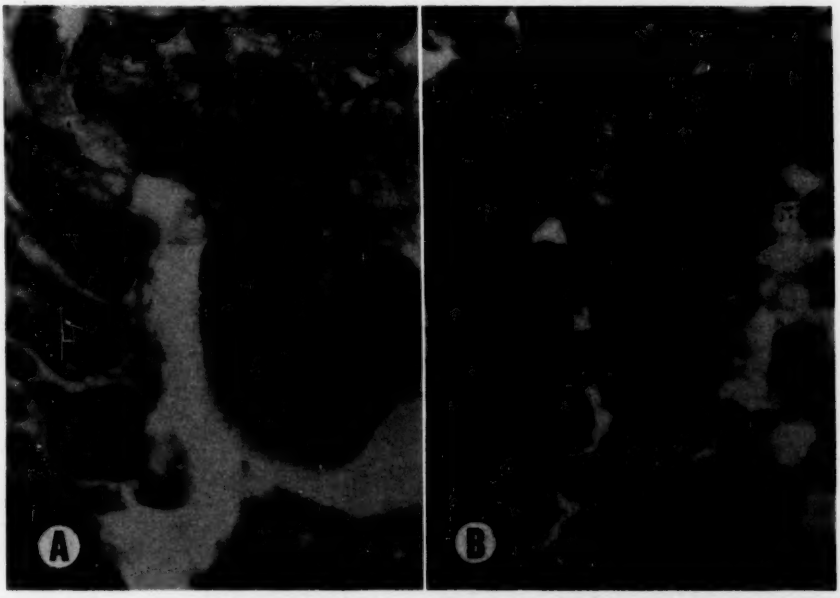

FIG. 3. Lung. A: Human. Bronchial lining epithelium with giant cell containing 2 inclusions indicated by arrows. Stain: Phloxin-tartrazine. B: Ferret. Pulmonary lining epithelium with many dark staining inclusion bodies. Stain: Picro-Mallory.

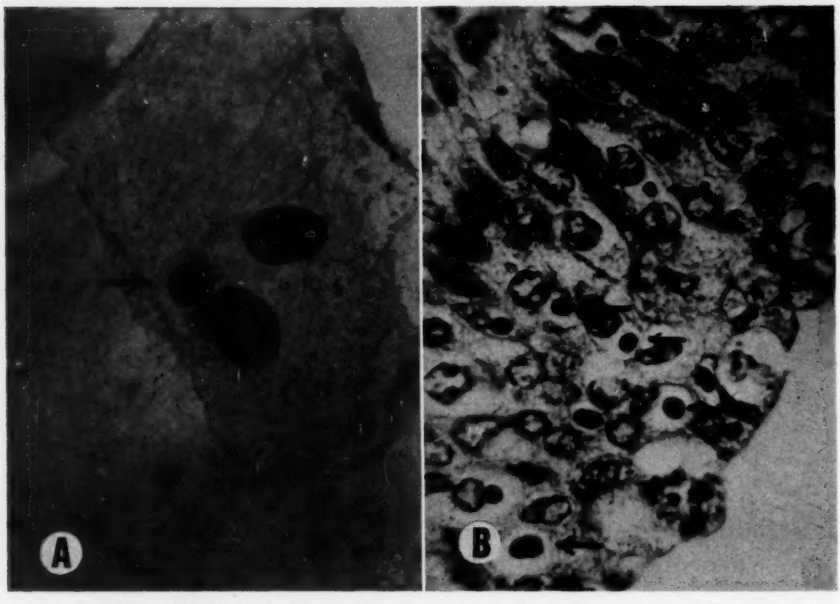

FIG. 4. Urinary Bladder. A: Human. Smear of epithelial cells from urinary sediment showing large cytoplasmic inclusion body. Stain: Hematoxylin-Eosin. B: Ferret. Section from bladder of ferret which died of distemper showing many cytoplasmic inclusion bodies in epithelial lining cells. Stain: Picro-Mallory.

Experiments 1 and 2: Ferrets were inoculated subcutaneously with canine distemper virus (40% dog spleen) in 3 groups. Group I consisted of 5 animals which were given 0.1 cc. virus only. Group II consisted of 5 animals which were inoculated with 3 cc. hyperimmune distemper antiserum and 0.1 cc. virus. Group III with 5 animals received 3 cc. human gamma globulin and 0.1 cc. virus. Differences between the groups were not striking except that animals in Group III lived twice as long as those in Groups I and II after the onset of disease. These results suggested that the dose of virus was overwhelming and that there might have been some protective substance in human gamma globulin.

Experiment 3: A litter of 8 young ferrets were inoculated subcutaneously with distemperoid virus 0.1 cc. 1:100 dilution. Group I, 3 animals, received virus only; Group II, 2 animals were inoculated with hyperimmune distemper antiserum 0.5 cc./animal on 1st, 3rd, 7th, 10th, 13th, 16th and 27th days following virus inoculation; Group III, 3 animals received human gamma globulin 0.5 cc./animal and virus on the same days as the above group. In Control Group I, the 1st animal became ill with typical distemper on 14th day; the other 2 became ill on the 17th day. The animals survived 3 to 5 days after the onset of illness and were all dead before any of those in the other groups became ill. In Group II, the 1st animal became ill on the 26th day following virus inoculation and died in 3 days. The largest animal of the litter in this group became ill on the 31st day and was killed at the end of the experiment. In Group III the 1st animal showed signs of illness on the 27th day, the 2nd on the 31st day and the 3rd animal remained well until the end of the experiment on the 35th day. There appeared to be a definite sparing effect in this experiment demonstrated by the hyperimmune serum and by human gamma globulin, the latter showing an equal or better protective effect. (See chart 1.) This result of in vivo neutralization led to a further trial of the effect of in vitro neutralization reported in the following experiment.

Experiment 4: Nine young ferrets were inoculated subcutaneously with mixtures of virus and immune serum or human gamma globulin. Group I, 3 animals received 1.0 cc. of a 1:10,000

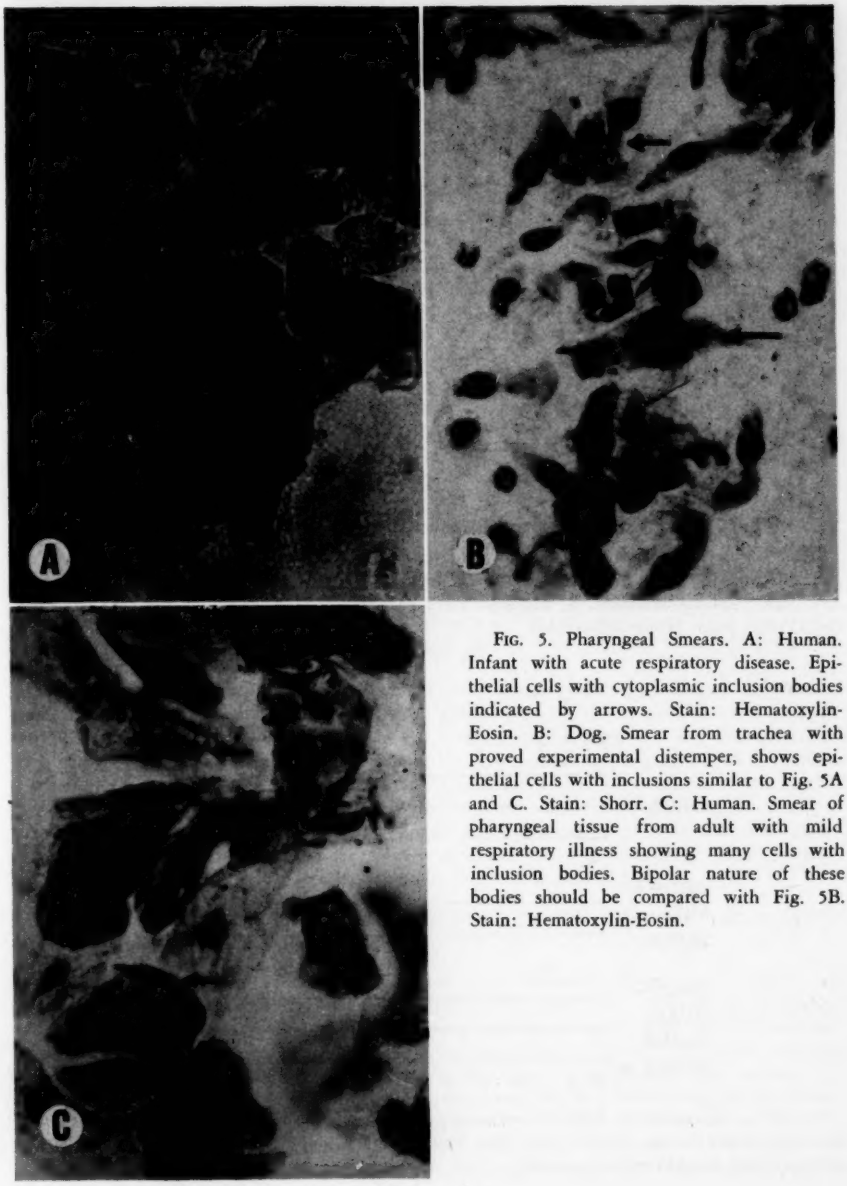

FIG. 5. Pharyngeal Smears. A: Human. Infant with acute respiratory disease. Epithelial cells with cytoplasmic inclusion bodies indicated by arrows. Stain: Hematoxylin-Eosin. B: Dog. Smear from trachea with proved experimental distemper, shows epithelial cells with inclusions similar to Fig. 5A and C. Stain: Shorr. C: Human. Smear of pharyngeal tissue from adult with mild respiratory illness showing many cells with inclusion bodies. Bipolar nature of these bodies should be compared with Fig. 5B. Stain: Hematoxylin-Eosin.

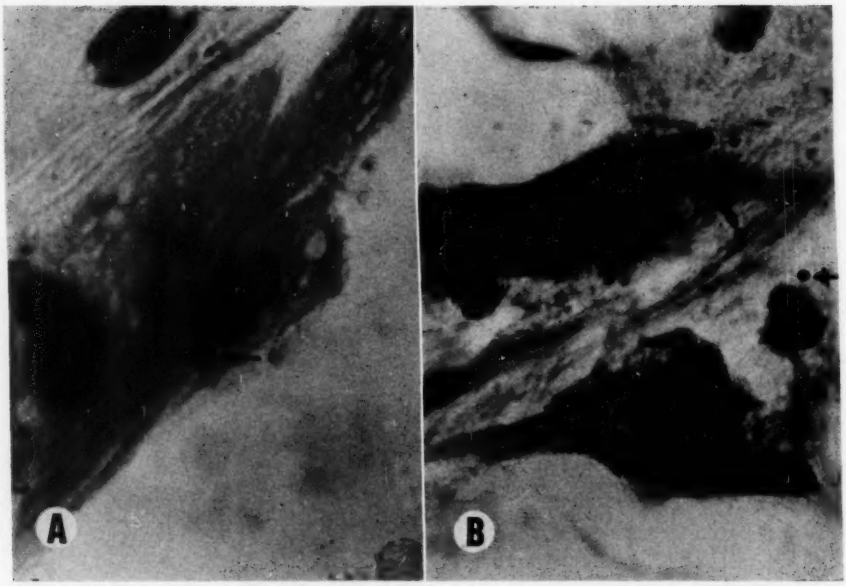

FIG. 6. Pharyngeal Smears. A: Monkey. First passage, 11 days following inoculation intranasally and pharyngeally from human patient with pneumonitis showing inclusion body in epithelial cell. Stain: Phloxin-tartrazine. B: Monkey. Third passage, showing many inclusion bodies in epithelial cells. Stain: Hematoxylin-Eosin.

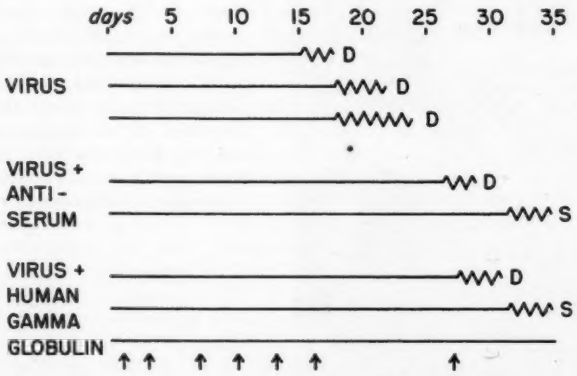

CHART 1. Experiment 3. Each line represents animal and illustrates ferret's illness with day of onset and death; arrows indicate days when human gamma globulin and hyperimmune distemper antiserum were given to respective animals.

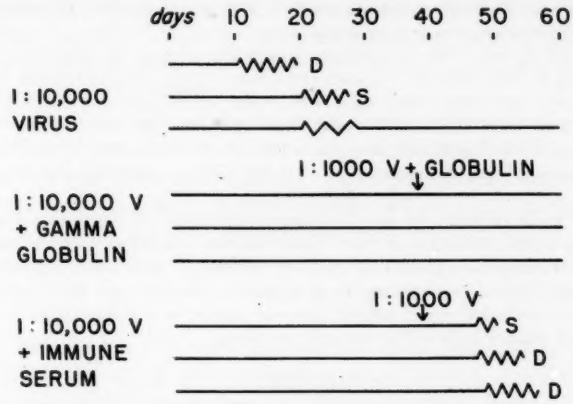

CHART 2. Experiments 4 and 5. Each line represents animal and illustrates onset and course of illness in unprotected animals given virus only. Animals receiving human gamma globulin remained well throughout experiment although intimately exposed to sick animals which were in same tier of cages. At 38th day, Experiment 5 was started on remaining 6 animals, and illustrates onset and course of illness of unprotected animals in lower section given virus only.

suspension of ferret spleen virus.* Group II, 3 animals received a similar amount of virus plus 1.0 cc. human gamma globulin and Group III, 3 animals received the virus plus 1.0 cc. ferret immune serum.* All 3 animals in Group I became ill, one died, one was killed and one recovered. Typical inclusion bodies as seen in proved distemper were demonstrated in autopsy or from biopsy material. The other 6 animals remained well and were the subjects of the next experiment which was similar to the above Experiment 4, except that a much larger dose of virus was used to test the protective effects of gamma globulin. (See chart 2.)

Experiment 5: Six animals inoculated with 1.0 cc. ferret spleen virus diluted 1:1,000. In 3 animals this dose was mixed with 1.0 cc. human gamma globulin. The animals receiving globulin remained well and the other 3 sickened on 6th and 7th days and died in 3 to 4 days with distemper. This experiment demonstrated again a solid protection of ferrets by human gamma globulin against a relatively large dose of virus. The results of Experiments 4 and 5 are illustrated in chart 2.

Virus neutralization tests were performed in chick embryos with chick embryo-adapted distemper virus (Lederle strain) on several samples of human sera.† The results of these tests will not be reported here,[13] but they demonstrated the property of neutralization by adult serum and the lack of neutralization by serum of the infants tested and by serum of normal ferrets.

Two patients in which paired sera showed a significant difference will be briefly reviewed here.

Case 1. A 10 yr. old boy was admitted to University of Minnesota Hospital with an acute respiratory illness which began 10 days following the death of his puppy from distemper. A pharyngeal smear biopsy on admission revealed an occasional rare inclusion body, less than one/200 epithelial cells. Two days later at the height of his illness pharyngeal smear contained 10 positive cells/200 counted. At this time a roentgenogram of chest revealed signs of pneumonitis. His recovery was uneventful. Acute and convalescent serum samples were tested for their neutralizing properties and neutralization was demonstrated in the acute specimen at 1:10 dilution of serum but not at 1:100 dilution. Two convalescent specimens from the patient, taken months apart, showed neutralization at 1:100 dilution of patient's serum, but not at 1:1,000 dilution. These sera were inactivated by heating

* Supplied by the Lederle Laboratories.

† These tests were performed at the Lederle Laboratories at Pearl River through the kindness of Drs. Herald Cox and Victor Cabasso.

to 56°C. for 30 min. Tests were performed with a 40% suspension of chorioallantoic membrane which undoubtedly represents a very large dose of virus.

Case 2. A 4 yr. old boy, while convalescent from poliomyelitis in an institution in Minneapolis, became ill during a small epidemic of acute respiratory disease. His temperature rose to 39.5°C. He complained of a sore throat and cough. WBC count on that day was 8,600/m³; polymorphonuclears 62%, lymphocytes 36% and mononuclears 2%. His temperature rose the next day to 40.0°C. following which it gradually declined to normal in 3 days, rose to 39.0°C. the next day, then remained normal. Chest RG taken on the 3rd day of illness showed a diffuse infiltration of L lung field.

A pharyngeal smear taken on 5th day of illness revealed 11% of the epithelial cells with cytoplasmic inclusion bodies. The early or acute blood specimen was drawn the next day and the late or convalescent specimen was obtained on 24th day of illness. Tests for influenza A and B antibodies were negative, and cold-agglutinin test was negative.

The acute and convalescent serum samples from this patient were tested against canine distemper virus, chick embryo adapted strain and are recorded in table 1.

TABLE 1

APPROXIMATE TITER OF ACUTE SERUM AS EXPRESSED BY CALCULATED DILUTION OF SERUM WHICH PROTECTS 50% OF EMBRYOS AGAINST 25 ID_{50} OF VIRUS WAS 1:15. TITER OF CONVALESCENT SERUM WAS 1:640

Serum Dilutions	Acute Serum		Convalescent Serum	
	Growth on Membrane # of Eggs	No Growth on Membrane # of Eggs	Growth on Membrane # of Eggs	No Growth on Membrane # of Eggs
1:10	2	3	0	6
1:40	4	1	0	5
1:160	6	0	0	5
1:640	5	0	2	2

The results indicate no evidence of neutralization in acute specimen and complete neutralization in convalescent specimen at dilutions of 1:160. A virus-suspension of 1:100 dilution was used in these tests, and sera were not inactivated.

Neutralization tests with human gamma globulin in mixtures with virus-suspensions of 1:100 showed complete inhibition of growth on the chorioallantoic membrane at 1:320 dilution of globulin. At 1:640 growth was present in 4 of 6 eggs. Control test of virus-suspension at 1:100 suspension showed a good growth in 5 of 6 eggs. This experiment was repeated with inactivated gamma globulin (heating to 56°C. for 30 min.) with the following results: At 1:160 dilution of gamma globulin growth was present on 2 of 6 eggs; at 1:320 dilution, growth was present on 1 of 5 eggs; at 1:640 all 5 eggs showed growth. These results are comparable. With a 40% suspension of egg-virus, gamma globulin neutralized the infection in 11 eggs in dilutions of 1:10, 1:20 and 1:25 but failed to do so completely at the 1:50 dilution of gamma globulin. A good growth of lesions was evident in the eggs in which a 1:100 dilution was employed.

DISCUSSION

Experimental data have been presented which indicate a possible direct relationship between a proved viral disease of dogs (distemper) and a respiratory disease of human beings (primary pneumonitis[1-4]). Comparative pathologic material shows a striking similarity in morphologic characteristics in the human and animal tissues. Apart from the inclusion bodies, these changes appear identical. The staining properties of the inclusion bodies have also been shown to be identical. Serologic neutralization of canine distemper in ferrets and in living chick embryos is further definite evidence. Neutralization has

been demonstrated in both in vivo and in vitro experiments. The dose of virus employed appears to play an important role in the neutralization results. The neutralizing properties of human gamma globulin have been shown to be as high as hyperimmune distemper antiserum in the in vivo experiments.

The disease picture of distemper in dogs and ferrets is clinically comparable to the human respiratory disease under study, particularly when revealed in its purest forms. The experimental disease in the ferret and dog cared for in strict isolation is characterized by a febrile disease involving the respiratory passages with a biphasic temperature curve.[6] When treated with antibiotics, the disease may be studied in the animal in what appears to be an uncomplicated form. A great deal more study of the human disease in all its aspects is needed with transmission experiments from man to animals. These are now in progress.

Pharyngeal inclusions *per se* have no diagnostic significance and are subject to the same interpretation as we now give to the ever-present bacteria in the naso-pharyngeal areas. Recent reports[14–16] ascribe no specific significance to these findings. If these bodies represent a change in the cell due to invasion by an infectious agent (as is well established in many viral diseases, including rabies, distemper, variola, etc.), then we may be dealing with a very ubiquitous agent. Andrewes[17] states, "Many viruses, perhaps most, normally exist as inapparent or latent infections." There is evidence that man is a carrier of bacterial, viral and fungal agents; and there is also evidence of the vertical transmission of viruses. It is possible that other agents may produce inclusions in cells or that they represent degenerative changes only. However, identical changes in epithelial cells are produced by a proved virus disease (distemper).

In spite of the evidence from the accompanying morphologic and serologic data, the limitations of each are such as to indicate the need for further study before the two diseases can be said to have a similar etiology.

Summary

Clinical, epidemiologic, pathologic and serologic evidence has been presented which indicates a possible relationship of canine distemper and a respiratory disease of human beings.

Neutralization of distemper viral infection in ferrets has been accomplished experimentally; infection caused by this virus in living chick-embryos has been neutralized by human sera and by human gamma globulin. Both in vivo and in vitro methods were employed in these experiments.

Inclusion bodies are shown with the same morphologic and staining characteristics as well as similar tissue reactions to infection. The striking features of these changes are the proliferation and destruction of pulmonary lining epithelium, giant cell formation, and a predominant mononuclear reaction in the animal and human sections.

A review of the literature on a possible relationship between canine distemper and human illness has been presented. The former disease is now proved to be due to a specific virus.

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SPANISH ABSTRACT

Estudio Comparativo del Moquillo Canino con una Enfermedad Respiratoria del Hombre

En 1941, se describió una nueva modalidad de enfermedad epidémica respiratoria que ocurría en niños prematuros y lactantes pequeños.

El cuadro clínico era similar pero variaba en severidad desde una forma ligera con tos y estornudos de moderada intensidad a una forma severa con tos intensa, disnea y cianosis terminando con la muerte en todos los casos de la epidemia. La curva térmica era bifásica. La enfermedad era altamente contagiosa particularmente en las salas hospitalarias en donde fué primeramente estudiada y por primera vez se describió en seres humanos con una enfermerad respiratoria epidémica, lesiones histopatológicas caracterizadas por proliferación y destrucción del epitelio pulmonar de revestimiento, exudado mononuclear predominante y cuerpos de inclusión característicos. Este síndrome ha sido observado esporádicamente y en la actualidad existe evidencia creciente de que puede ocurrir en forma moderada o inaparente con cierta frecuencia, en seres humanos y con todas las variedades de intensidad clínica así como con diferencias apreciables en la morbilidad y mortalidad entre prematuros y niños a término. Los prematuros, que probablemente representan al huesped humano mas sensible, eran los mas seriamente enfermos y todos los grados de intensidad, hasta los moderados o de infección inaparente ocurrieron en lactantes mayores o niños.

La revisión de la literatura muestra que desde antes de que Laidlaw y Dunkin comprobaran que el moquillo o gripa canina era causado por un virus; ya Jenner, mas de un siglo antes, hacia su comparación con las fiebres infecciosas humanas, pero fué Nicolle quien por primera vez reporta pruebas experimentales de la relación entre este padecimiento canino y una infección humana al lograr la transmisión del padecimiento al hombre en una forma inaparente. Ademas se han reportado otros casos en que existen pruebas circunstanciales evidentes de una relación íntima entre casos probados de moquillo canino e infecciones de las vias respiratorias en el hombre.

Por otra parte, la descripción clínica de la gripa canina es similar a la citada arriba: enfermedad de alta contagiosidad, cuya manifestación mas constante es una curva febril de caracter bifásico, de alta mortalidad en la forma epidémica, a veces complicada con síntomas neurológicos. Asímismo, las lesiones histopatológicas son muy similares a las descritas por el autor de este artículo en los pulmones humanos y en monos con moquillo experimental, incluyendo la presencia de cuerpos de inclusión en el sedimento urinario humano de varios pacientes similarmente a los que ocurren en las celulas de revestimiento del tracto urinario de los animales con moquillo.

Finalmente, el autor realiza con éxito una serie de experimentos de neutralización en monos experimentalmente infectados con virus de la gripa canina y logra neutralizar la infección causada por este virus en embriones vivos de pollo por medio de suero humano y gammaglobulina humana, usando estos métodos tanto in vivo como in vitro en dichos experimentos. Así demuestra que las propiedades neutralizantes de la gammaglobulina humana son tal altas como las del suero hiperinmune contra el moquillo en los experimentos in vivo.

El autor concluye que a pesar de las pruebas aportadas por estos datos morfológicos y serológicos, sus limitaciones son tales que indican la necesidad de mas estudios antes de afirmar que ambos padecimientos tengan una etiología similar.

University of California Medical Center

CONGENITAL DISLOCATION OF THE HIP

Diagnosis and Natural Course

By GEORGE W. PLUMMER, M.D.

CONGENITAL dislocation of the hip is a serious and not infrequent deformity and is one of the few congenital malformations which can be treated with hope of a complete recovery; however, the diagnosis must be made early in life and adequate therapy must be carried out in order to effect a complete cure. As pointed out by Hart[1] and more recently by Pray,[2] the recognition of this condition is the responsibility of the pediatrician and general practitioner.

This paper is concerned with the evaluation of clinical signs of congenital dislocation of the hips. The study was carried out on 227 infants, 9 months of age, who were born in Hiroshima, Japan.

The circumstances of this investigation afforded a unique opportunity (1) to determine the reliability of the physical signs of congenital dislocation of the hip, (2) to follow the natural course of this deformity and (3) to make some observations on the pathogenesis of the condition.

METHODS AND MATERIALS

At the time this study was done approximately 50% of the infants born in Hiroshima were being examined at 9 mo. of age in the laboratories of the Atomic Bomb Casualty Commission. Two hundred twenty-seven 9 mo. old infants (118 males and 109 females) seen on 12 consecutive examining days were studied. Each infant was examined by an American pediatrician.

The presence or absence of the following was recorded: (1) asymmetry of the adductor thigh creases; (2) limitation of abduction of the flexed thigh; (3) the "click" sign of Ortoloni.

These criteria were chosen because it was thought that they were objective signs and were easy to elicit. The first observation on thigh creases was made with the infant lying in the normal anatomic position; the other two while performing the Ortoloni maneuver of abduction of the flexed thighs as described by Hart.[1] This maneuver is performed by first flexing the thighs, adducting them slightly, then abducting them while they are still flexed. The positive signs suggestive of hip pathology which may be elicited by this maneuver are limitation of abduction caused by contracture or spasm of the adductor muscles and the click or jerk which is produced when the dislocated femoral head slips suddenly over the cartilaginous rim of the acetabulum into normal position. Hart[1] considers this latter sign pathognomonic of congenital dislocation of the hip.

A single AP RG of the pelvis was taken on each infant following the physical examination. All films were interpreted by the Commission's radiologist.*

RESULTS OF THE INITIAL EXAMINATION

Table 1 summarizes the results of the clinical and roentgen findings on these 227 nine month old infants.

Asymmetry of the adductor thigh creases was noted in 81 instances with approximately equal distribution between the sexes. The cephalad crease was found on the right

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TABLE 1

INCIDENCE OF POSITIVE CLINICAL FINDINGS IN 227 NINE MONTH OLD INFANTS WITH REGARD TO DISLOCATION OF HIP

Sex	No.	Asymmetry of Thigh Crease		Limitation of Abduction		Click	Abnormal RG	
		No.	Per Cent	No.	Per Cent		No.	Per Cent
Female	109	37	33.9	21	19.2	3	20	18.3
Male	118	44	37.2	23	19.5	1	7	5.9
Total	227	81	35.6	44	19.4	4	27	11.8

side in 41 infants and on the left in 40. Limitation of abduction of the flexed thighs was noted in 44 infants. The limitation was bilateral in 10 cases and unilateral in 34, with the right side involvement occurring more than twice as often as the left. The click or jerk of entry was felt to be present in four infants.

A study of 227 roentgenograms revealed 27 infants with abnormal hip joints. Fifteen of the 27 infants had roentgenograms which were interpreted as showing questionable or potential abnormalities of the hips, characterized only by lack of calcification of the oblique acetabular roof. The remaining 12 cases were interpreted as definite dislocation or subluxation of the hip.

TABLE 2

CORRELATION OF CLINICAL AND ROENTGENOGRAPHIC FINDINGS IN 27 NINE MONTH OLD INFANTS WITH REGARD TO DISLOCATION OF HIP

Roentgenographic Interpretation		Clinical Evaluation				
		Asymmetric Skin Crease	Limitation of Abduction	Combination of Both	Click	Negative
Definite	12	2	1	2	2*	5
Potential	15	2	1	1	0	11
Total	27	4	2	3	2	16

* One had limitation of abduction and one had asymmetric thigh creases in addition to the click sign.

Table 2 shows the correlation between the clinical and roentgen findings in these 27 patients. It is interesting to note that 16 of the 27 infants with positive roentgen findings had no demonstrable clinical evidence of hip disease, using the physical examination criteria described above.

It is evident from tables 1 and 2 that discrepancies existed between the clinical and roentgen findings. The high incidence of asymmetric thigh creases was anticipated. The lack of correlation between this finding and roentgen evidence of hip pathology suggests that the value of this sign is that it serves as a reminder to the physician of the entity, congenital dislocation of the hip. The large number of cases with limitation of abduction was also anticipated; undoubtedly many of these were due to voluntary contraction, although the examiner tried to evaluate the patient from this standpoint. But the ab-

TABLE 3

RESULTS OF PHYSICAL AND ROENTGENOGRAPHIC EXAMINATION ON 26 INFANTS AT 9 MONTHS AND 18 MONTHS WITH REGARD TO HIP

Case No.	Sex	First Examination		Second Examination	
		Physical	Roentgenogram	Physical	Roentgenogram
			Group I		
1	Female	Negative	Questionable dislocation, bilateral	Negative Walks normally	Normal
2	Male	Asymmetry of thigh fold	Potential dislocation, left	Negative Walks normally	Normal
3	Female	Negative	Potential dislocation, bilateral	Negative Walks normally	Normal
4	Female	Negative	Potential dislocation, bilateral	Negative Walks normally	Normal
5	Female	Negative	Potential dislocation, bilateral	Negative Walks normally	Normal
6	Female	Negative	Potential dislocation, bilateral	Negative Walks normally	Normal
7	Female	Negative	Potential dislocation, bilateral	Negative Walks normally	Normal
8	Female	Negative	Potential dislocation, bilateral	Negative Walks normally	Normal
9	Female	Negative	Questionable dislocation, bilateral	Adductor contracture on left. Cannot walk	Normal
10	Female	Negative	Potential dislocation, left	Negative Walks normally	Left acetabulum slightly deficient
11	Male	Asymmetry of thigh creases (?); limitation of abduction, bilateral	Potential dislocation	Contracture, bilateral Infant crying Walks normally	Normal
12	Female	Asymmetry of thigh creases	Potential dislocation, bilateral	Negative Walks normally	Normal
13	Female	Negative	Potential dislocation, right	Negative Walks normally	Normal
14	Male	Negative	Potential dislocation, left	Negative Walks normally	Normal
			Group II		
15	Female	Negative	Definite dislocation, left	Negative Walks normally	Femoral head, irregularly calcified; acetabulum slightly shallow on left
16	Male	Asymmetry of thigh crease, left	Definite dislocation, bilateral	Negative Walks normally	Probably normal, acebula still shallow
17	Male	Asymmetry of thigh creases	Definite dislocation of left; potential on right	Negative Walks normally	Left acetabulum poorly formed. Right normal
18	Female	Asymmetry of thigh creases	Definite dislocation on right	Negative Walks normally	Right acetabulum slightly deficient, probably normal
19	Male	Negative	Potential dislocation on left. Definite on right	Negative Walks normally	Definite dislocation on right. Left normal
20	Male	Negative	Left definite dislocation. Right potential	Negative Walks normally	Normal
21	Female	Asymmetry of thigh crease and limited abduction	Definite dislocation, right	Limited abduction on right	Right acetabulum abnormal but improved
22	Female	Negative	Left definite dislocation	Negative. Limp on left	Definite dislocation on left
23	Female	Limited abduction on right	Definite dislocation, bilateral	Limited abduction on right	Definite dislocation on right with left acetabulum
24	Female	Asymmetry of thigh crease on right. Click bilateral	Definite dislocation, bilateral	Limited abduction bilaterally Walks normally	Definite dislocation on right. Left normal
25	Female	Asymmetry on left. Limited abduction, bilateral. Click, bilateral	Definite dislocation, bilateral	Limited abduction, bilaterally. Unable to walk	Definite dislocation bilaterally
26	Female	Negative	Definite dislocation on right	Slightly limited abduction on right. Limp on right	Definite dislocation on right

sence of clinical signs in 16 cases out of 27 with roentgenographically abnormal hips was an unexpected finding.

These observations, coupled with the unexpectedly high incidence of roentgen findings of abnormal hips in this series of 227 infants (11.8%), suggested that follow-up studies should be done. The infants with potential subluxation were considered particularly interesting because of Hart's[1] statement that persistent potential subluxation or slight subluxation could be a frequent cause of hip disease of later life.

Twenty-six of these infants were returned at 18 months of age for repeat examinations (one infant had moved from the area). When the second physical examination was performed, the presence of asymmetric thigh folds was disregarded but a description of the walking ability was recorded. A second AP roentgenogram of the pelvis was also obtained. None of these infants had received treatment in the interim.

Results of 18 Month Examinations

The results of both the 9 and 18 month examinations on these 26 patients are summarized in table 3.

Group I: Cases 1 through 14 are those who had roentgen evidence of questionable or potential subluxation on the first examination. On the second examination at 18 months, only one of this group had an abnormal roentgenogram (Case 10), described as a slightly deficient acetabulum on the left. This patient's second physical examination was negative, and she walked well. Two patients in this group had abnormal findings at the physical examinations done at 18 months: Case 11 had bilateral limitation of abduction of the flexed thighs but walked well; Case 9 had limited abduction on the left and was unable to walk. The latter infant was retarded in other respects as well. Both infants had normal-appearing hips on the second roentgenogram. The remaining 11 infants of this group had no evidence of abnormality of the hips on either clinical or roentgen examination at this time. In other words, 13 of the 14 infants had during the 9 to 18 month period developed normal-appearing hips with well-calcified acetabula.

Group II: Twelve cases, 15 through 26, are those who were considered to have definite subluxation or dislocation on the 9 month roentgenogram. On the second clinical examination, 6 of these infants, Cases 15 through 20, had negative physical findings and walked normally. One of these 6, Case 20, had normal hips on the 18 month roentgenogram; on two others, No. 16 and 18, the 18 month roentgenograms were interpreted as probably normal, although the acetabula were described as slightly deficient. Two other cases of the 6 with normal physical examinations had abnormal hips on the second roentgenogram, but the pathologic changes were less marked than on the first examination. The last case of these 6, No. 19, had a definitely abnormal right hip, with questionable displacement of the femoral head.

In Group II, Cases 21 through 26 exhibited one or more signs of hip pathology on the 18 month physical examination. Two infants had limitation of abduction only; two had limitation of abduction of the flexed thighs and were unable to walk. One had a limp only and the last one of the 6 had a limp and limited abduction. The roentgenogram on one of the 6, No. 21, showed some improvement in the hip joint, although it was still abnormal at 18 months. The remaining 5 of these 6 cases, No. 22 through 26, showed definite dislocation or subluxation on the 18 month roentgenogram.

The 18 month examinations demonstrated better correlation between the roentgen findings and the physical signs. This is particularly true of the last six cases discussed

where in each instance there was some sign of hip pathology, on both physical and roentgen examinations. Limited abduction was the most constant sign and was present in 5 of the 6 cases. In only one of the 12 cases in Group II was there roentgen evidence of a definite, although slight, subluxation and negative physical examination at 18 months.

The subsequent spontaneous normal development in the patients in Group I and the improvement of many of those in Group II indicated that further follow-up studies should be done. Ten of the 12 cases in Group II were therefore recalled for repeat physical and roentgen examinations at 25 months of age (one case, No. 20, was not returned because the 18 month examination had been entirely normal, and the other case, No. 22, had moved from the area). The procedure at this time was the same as that described for the 18 month study.

Results of the 25 Month Examinations

The results of the physical and roentgen studies on these 10 children are summarized in table 4. Six had negative physical examinations and walked well at the age of 25

TABLE 4

Physical and Roentgenographic Examinations on 10 Infants from Group II at 25 Months of Age

Case No.	Sex	Physical Examination	Roentgenographic Examination
15	Female	Negative Walks well	Normal although left acetabulum is slightly less well formed than right
16	Male	Negative Walks well	Normal joints Slope of acetabula slightly increased
17	Male	Negative Walks well	Probably normal Left acetabulum is rough and has an increased slope
18	Female	Negative Walks well	Normal hips except for slightly irregular acetabulum
19	Male	Negative Walks well	Right acetabulum still shallow—head in normal position—progressing toward normal hip
21	Female	Negative Walks well	Normal hips although right acetabulum is slightly irregular
23	Female	Hips in plaster cast	Left hip normal Right hip dislocated
24	Female	Marked limitation of abduction on right	Right slope is increased Femoral head displaced
25	Female	Bilateral limitation of abduction Unable to walk	Hips dislocated bilaterally
26	Female	Limited abduction on right; definite limp on right	Right acetabulum poorly formed; femoral head small and displaced

months. One of these 6 had had limited abduction at the 18 month examination, but this had disappeared at the 25 month examination (Fig. 1). The other 5 had negative physical examinations at both times. The roentgenograms on 5 of the first 6 patients were interpreted by the radiologist as normal, or probably normal, although in each instance there was a slightly increased slope of the acetabulum or some irregularity of the calcification of the acetabulum, but in each instance, the femoral head was in essentially normal position. The roentgenogram of the remaining case of these first 6, No. 19,

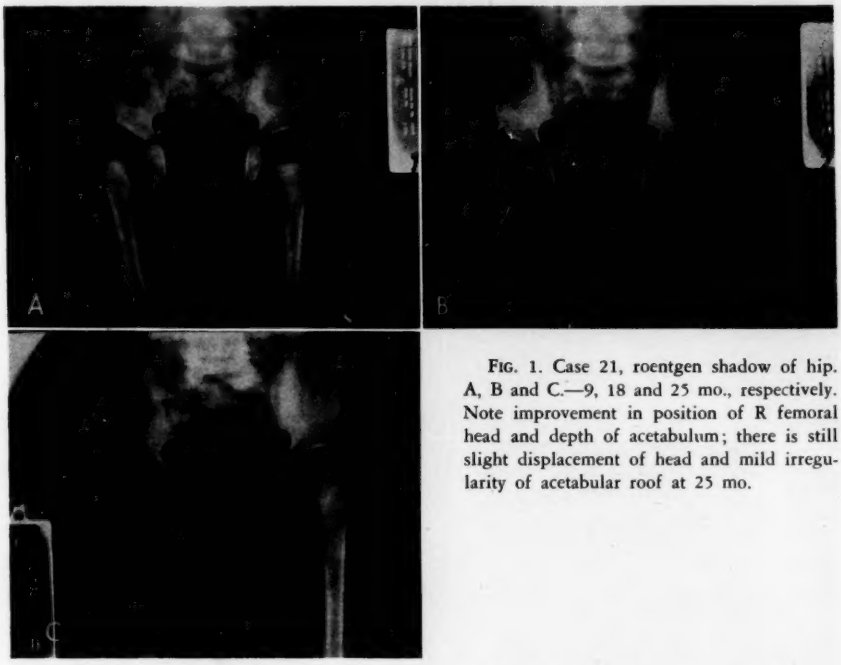

FIG. 1. Case 21, roentgen shadow of hip. A, B and C.—9, 18 and 25 mo., respectively. Note improvement in position of R femoral head and depth of acetabulum; there is still slight displacement of head and mild irregularity of acetabular roof at 25 mo.

demonstrated a shallow right acetabulum, but the head was in better position and was interpreted as progressing toward normal (Fig. 2).

The last patients all showed physical signs of hip disease and had roentgen findings of definite dislocations. One of these, Case 25, was in a plaster spica, and this individual was one of the two patients unable to walk at the time of the 18 month examination. The mother stated that the patient learned to walk with a limp after the 18 month examination and before the cast was applied. The other patients had marked limited abduction of the flexed thighs: one was unable to walk, one had a definite limp and one walked fairly well. The patient in the spica was the only one of the 10 who had received any treatment.

DISCUSSION

Incidence: The incidence of actual congenital dislocation of the hips in this series is 5 out of 227, or 2.2%, if only the four patients seen at 25 months with definite dislocation and the one who had definite dislocation at 18 months but did not return for the third examination are included. It is possible that some of these cases which had roentgen evidence of minor residual alteration in the acetabula at 25 months will continue to have

persistent changes which would place them in Hart's[1] group of presubluxation or slight subluxation. Therefore, these cases should be followed further. However, the author feels that in view of the absence of clinical signs, these hips will continue to progress toward normal.

Diagnosis: Limitation of abduction of the flexed thighs has been considered the most

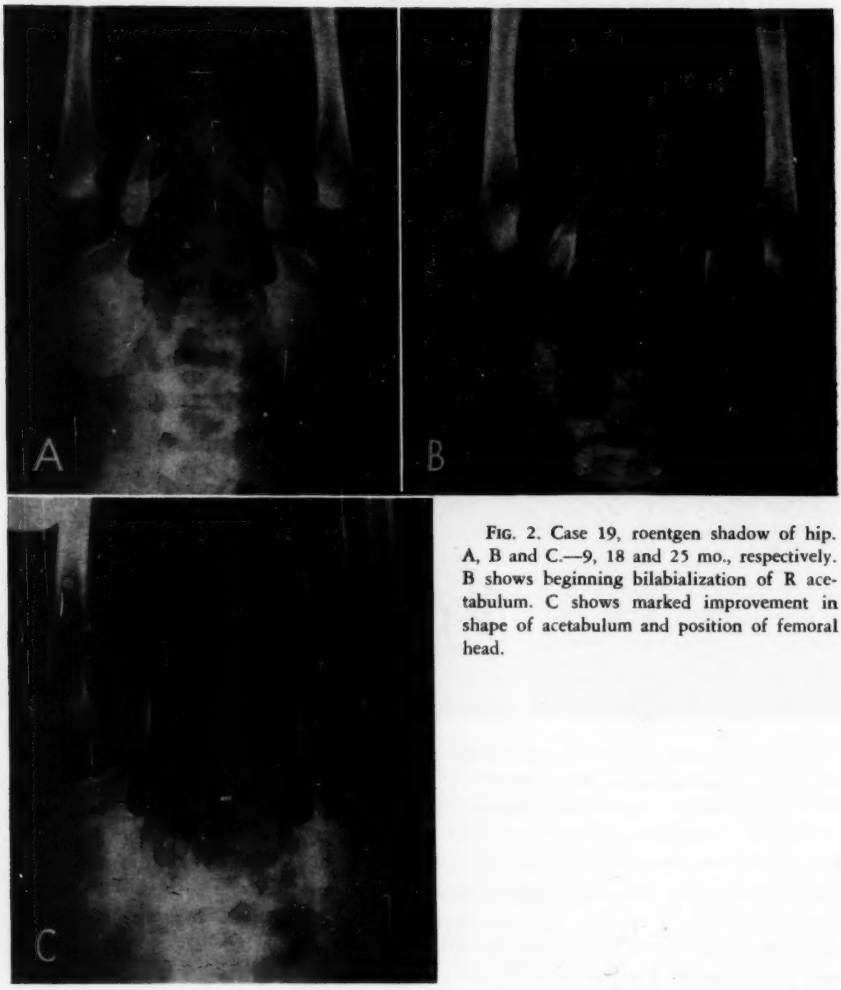

FIG. 2. Case 19, roentgen shadow of hip. A, B and C.—9, 18 and 25 mo., respectively. B shows beginning bilabialization of R acetabulum. C shows marked improvement in shape of acetabulum and position of femoral head.

consistent physical sign of congenital dislocation of the hip by other authors.[1,2] This proved to be true in the present study, particularly at the 18 month and 25 month examinations. It is possible that other patients in this series had physical signs, such as limited abduction of the thighs and/or the click sign in early infancy which had disappeared by the age of 9 months. Pray[2] mentions four young infants with clinical signs who were not treated because of equivocal roentgenograms and whose clinical signs disappeared within a 3 month period. It is interesting to note that two patients whose dis-

location persisted by roentgenogram did not have limitation of abduction at the 9 month examination, and one of these did not have it at the time of the 18 month examination. The reason for this is not apparent; however, Pray[2] reports the same phenomenon and suggests that the complete dislocation causes the splinting of the joint to disappear. The disappearance of the click sign at 18 months in the two cases who had it at nine months is not surprising. Hart[1] states that the click sign cannot be elicited until the adductor contracture or spasm is overcome and that in infants older than a few months, the contracture often cannot be reduced except by prolonged traction applied over a period of several days. This was not possible to do in the present series because of the limited time available for each observation.

The roentgenogram, of course, is indispensable to the accurate diagnosis of congenital dislocation of the hip. The roentgen signs of dislocated hip have been well described elsewhere and will not be considered in detail here, except to suggest that a deficiently calcified acetabulum alone, without displacement of the femoral head, should be interpreted with caution unless instability of the joint can be demonstrated by physical methods.

Natural Course and Pathogenesis: Hart[1] has suggested and Pray[2] has demonstrated that some infants with potential subluxation and slight subluxation cure spontaneously. In the present series, all those with potential subluxation and 7 of the 12 with definite subluxation at 9 months either healed completely or demonstrated marked improvement by 18 to 25 months of age without treatment. This experience has suggested to the author that the delayed acetabular calcification, in at least those with a potential subluxation, may represent a normal variation in skeletal growth pattern. In other words, those infants calcify their acetabula at rates which are normal for them but slower than the average. This conception is supported by the fact that no instability of the joint was demonstrated at the time of the 9 month physical examination in those patients with the potential subluxation. One must conclude that in those who had some displacement at 9 months and who cured spontaneously, the muscle and fibrous tissue support to the hip strengthened as the child developed, thereby forcing the femoral head into normal position. The ultimately normal appearance of the acetabulum is produced by the constant force exerted by the muscles and ligaments in holding the femoral head securely into the acetabular socket. This is in accordance with Wolff's law.

Dislocation or subluxation then is caused by an inadequacy of the muscular and fibrous tissue support of the hip joint. The author proposes that this lack of support is the primary physiologic defect in congenital dislocation of the hip which produces the anatomic abnormality in the bony structure of the joint. This view is supported by the fact that it is possible to diagnose congenital dislocation of the hip in the newborn—a period in which no calcification of the acetabulum can be demonstrated roentgenographically. The lack of clinical signs in the cases who "healed" spontaneously in this series also adds support to this thesis, because the physical signs of dislocation of the hip are produced by the failure of the supporting tissues of the hips to hold the femoral head in normal position and not upon any bony deformity or inadequacy of the acetabulum and femur *per se*. The absence of clinical signs in these patients indicated that adequate muscular and ligamentous support to the hip was present; therefore, the femoral head was securely held in normal position and a normal-appearing hip joint ultimately developed. It is entirely possible that these infants had poor tonus of the supporting tissues of the hip in early infancy which was responsible for the shallow acetabulum which was demonstrated roentgeographically at 9 months, but this weakness had been overcome and the hip joint was progressing

toward normal development by the time the infant was first studied. In any case it seemed evident that faulty support of the hip by its musculo-ligamentous tissues is the basic defect responsible for the clinical picture of congenital dislocation of the hips, rather than any intrinsic fault in the osteogenic mechanism of the bony parts. While this theory is perhaps of academic importance, it does serve to re-emphasize the fact that early support to the dislocated hip is the only therapy which will give some promise of ultimate normal development of the joint.

Therapy: No comment on treatment can be made in the present series. Many of these infants would not have had attention called to their hips in practice since they had no clinical signs at 9 months of age. The serious disability produced by congenital dislocation of the hip forces the physician to treat all cases, potential or definite, which come to his attention. However, in view of the large percentage of spontaneous cures reported in this series, it seems evident that therapy should be employed, such as a Frejka splint, which supports the hip joint but does not immobilize the developing infant. The design and use of this splint has been described in detail by Hart.[1]

Summary and Conclusions

Physical and roentgen examinations were performed on 227 nine month old Japanese infants to discover all cases of congenital dislocation of the hip. Twenty-seven cases were found in which the roentgenograms of the hips were interpreted as abnormal; of these, 15 showed only lack of calcification of the acetabular rim, and the other 12 showed some degree of displacement of the femoral head, in addition to the deficiently calcified acetabulum.

A large percentage of these 27 infants had no physical signs relative to hip deformity.

Repeat examinations at 18 months and 25 months of age demonstrated that all infants with only deficient acetabular calcification and 7 of 12 with some displacement of the femoral head had either healed completely or showed marked improvement without treatment. Five cases had persistent and aggravated dislocation of the hip.

Limitation of abduction of the flexed thighs is the most consistent and valuable sign of congenital dislocation of the hips, and this is in accord with other investigators' conclusions.[1,2]

It is proposed that inadequate muscular and ligamentous support to the hip joint is the primary physiologic defect in congenital dislocation of the hip. This view is important in that it serves to direct attention to the fact that early support to the hip without immobilization of the infant is the most desirable therapy—from a physiologic standpoint—which will prevent deformity of the bony parts of the joint.

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Spanish Abstract

Luxación Congénita de la Cadera
Diagnóstico y Evolución Natural

Con objeto de evaluar los signos clínicos de la luxación congénita de la cadera se hizo en este estudio la revisión de 227 niños japoneses de 9 meses de edad buscando la oportunidad de determinar la significación real de los signos físicos, observar el curso espontáneo de la deformidad y hacer algunas observaciones acerca de la patogenia de este padecimiento.

Los niños fueron examinados a los 9 meses, a los 18 y a los 25 meses registrando si existía o nó cualquiera de los 3 datos siguientes: asimetría de los pliegues de adducción del muslo, limitación de la abducción cuando se flexiona el muslo y el signo del crujido de Ortoloni cuando la cabeza femoral dislocada resbala súbitamente sobre el borde cartilaginoso del acetábulo y se coloca en su posición normal. Durante el primer examen a todos los niños se les tomaron radiografías de sus articulaciones coxofemorales.

Los hallazgos fueron los siguientes: 27 casos de los 227 niños examinados por primera vez, mostraron placas radiológicas de las articulaciones coxofemorales que se interpretaron como anormales, 15 por falta de calcificación del anillo del acetábulo y 12 por cierto grado de desplazamiento de la cabeza femoral, ademas de calcificación deficiente del acetábulo. A la exploración física un gran porcentaje de estos 27 niños no tenían signo alguno de anormalidad de la articulación de la cadera.

Cuando este grupo se examinó nuevamente a los 18 y a los 25 meses sucesivamente se demostró que todos aquellos niños que tenían exclusivamente calcificación acetabular deficiente mas 7 de los 12 que tenían además cierto desplazamiento de la cabeza femoral habían curado por completo o bien mostraron mejoría acentuada sin ningun tratamiento y solamente los 5 casos restantes tenían luxación persistente de la cadera que se había agravado.

La conclusión del autor en cuanto a diagnóstico de la luxación es de que el signo mas persistente y valioso es el de la limitación de la abducción de los muslos flexionados, lo cual está de acuerdo con las conclusiones de otros autores debiéndose ser cauto en la interpretación radiológica de acetábulo deficientemente calcificado si no existe desplazamiento femoral, a menos que se compruebe por exploración física la inestabilidad de la articulación.

En cuanto a la patogénesis de la malformación parece ser que el defecto fisiológico primario es la falta de sosten muscular y ligamentoso de la articulación coxofemoral el cual secundariamente produce la anormalidad anatómica de la estructura ósea de la articulación.

Este punto de vista está sostenido por la observación bien comprobada de que es posible diagnosticar la luxación congénita de la cadera en el recién nacido precisamente cuando no se puede ver a los rayos x calcificación del acetábulo, y además, por la falta de signos físicos en los casos de este estudio que curaron espontáneamente, lo cual comprueba que dichos signos de la dislocación coxofemoral son producidos por la imposibilidad de los tejidos de sosten de la articulación para mantener la cabeza femoral en posición normal y no por deformidad o incapacidad del acetábulum y del femur por si mismos. Es muy posible que este grupo de niños tuvieran un tono muy pobre de los tejidos articulares de sosten durante su infancia temprana lo cual fué responsable del acetábulum superficial que se encontró radiológicamente a los 9 meses pero dicha debilidad fué desapareciendo y la articulación continuó su desarrollo normal posteriormente.

El hecho demostrado por otros autores de que algunos niños con subluxación potencial y subluxación ligera curen espontáneamente, también observado en este estudio, sugiere que el retardo en la calcificación del acetábulo, cuando menos en aquellos casos con subluxación potencial, signifique una variación normal del patrón de crecimiento del esqueleto, es decir, que estos lactantes calcifican su acetábulo a un ritmo que es normal para ellos pero mas lento que para el patrón promedio.

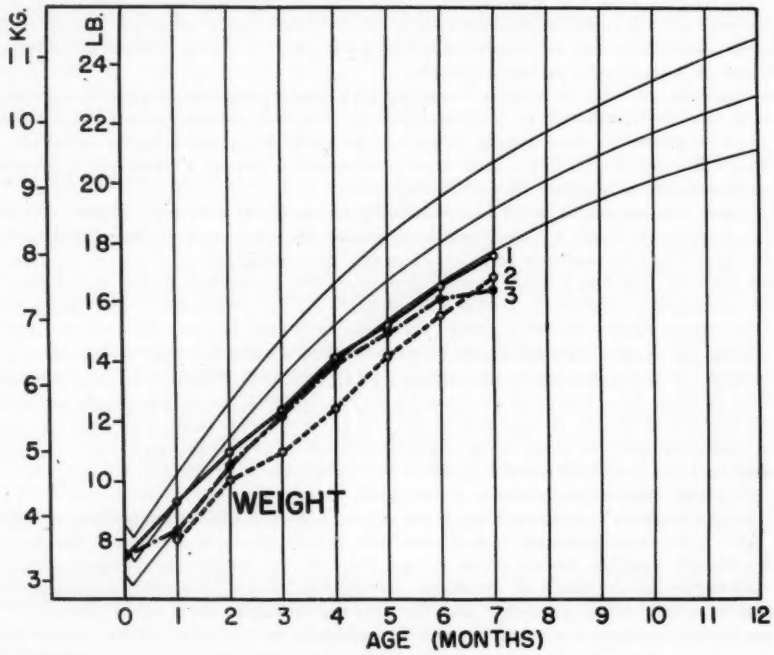
Este concepto patogénico de la malformación es importante pues llama la atención sobre el hecho de que el sosten temprano de la articulación sin inmobilización del niño es la terapéutica mas deseable, desde el punto de vista fisiológico, para prevenir la deformidad de las partes óseas de la articulación.

Atomic Bomb Casualty Commission

PATTERN OF GROWTH OF SELECTED GROUPS OF BREAST-FED INFANTS IN IOWA CITY

By SILVIO L. PAIVA, M.D.
Iowa City, Iowa

THE superiority of human milk in the feeding of infants has been undisputed throughout the years. Artificial feeding of infants in this country has become easy and successful and the incidence of breast feeding has decreased rapidly.[1-3] However, maternal



GRAPH 1. Comparison of weight curves of 1897 and 1910 groups of breast-fed and artificially fed infants with present standards.
1. Koplik's breast-fed group (1910)
2. Koplik's artificially fed group (1910)
3. Holt's breast-fed group (1897)

nursing is still considered the method of choice despite all the progress in artificial feeding.[3-8]

Human milk from a well fed mother contains all the required nutrients for the proper growth of the infant with the exception of a few food elements that may be added as

From the Department of Pediatrics, College of Medicine, State University of Iowa, Iowa City, Iowa.

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TABLE 1A

BREAST-FED BOYS; HEIGHT IN INCHES

	Birth	1 mo.	2 mo.	3 mo.	4 mo.	5 mo.	6 mo.	7 mo.
	20.5	22.0	23.0	24.3	25.2	26.1	26.8	27.0
			22.7	24.5	25.6	26.4		
		20.9	22.4	23.5	24.6	25.4	26.2	
	19.8	22.0	23.3	24.5	25.6	26.7	27.1	
		20.7	22.2	23.6	24.5	25.5	26.4	
	19.3	21.5	22.3	23.2	24.6	26.0	26.4	
	20.0	21.5	22.5	23.8	24.8	25 8		
			23.4	24.4	25.2	26.3	26.4	27.3
	19.7	21.1	22.4	23.8	24.8	25.5	26.0	
	20.0	21.2	22.6	24.0	25.1	26.0		
	20.0	21.8	23.6	24.6	25.4	26.1	26.9	
	19.7	21.0	22.5	24.0	24.7	25.6	26.7	27.4
	19.7	21.3	23.2	24.2	25.2	26.4	27.3	28.2
	19.2	20.0	21.5	22.5	24.0	25.2	26.5	
	20.5	22.0	23.7	24.7	25.5	26.2	27.5	28.0
	20.5	22.0	22.7	24.7	25.2	25.7	26.7	
	20.5	21.5	22.7	24.5	25.5	25.5	26.0	
		23.0	24.2	25.2	26.5	26.5	27.0	
	19.7	21.2	22.5	23.7	24.5	25.7		
	19.7	23.0	24.0	24.7	25.5	27.7		
	20.0	22.2	23.0	24.5	25.2	26.2		
N	16	19	21	21	21	21	15	5
M	19.93	21.56	22.9	24.15	25.11	26.01	26.66	27.58
S.D.	.41	.87	.68	.62	.54	.64	.57	

supplemental feeding to the infant's diet at the proper time throughout infancy.[4,9] Human milk is easily available and free of harmful bacteria.[4,5] The mortality during the first few months, according to most statistical studies, is lower among infants entirely breast fed.[4,10,11] Also fewer infections are reported in breast-fed infants compared with the artificially fed infants.[4,5,12,13] Finally much has been said concerning the psychologic aspect of breast feeding in the infant and the mother.[3,5,7,8] Successful breast feeding is usually a satisfactory experience for both mother and infant. This emotional satisfaction is considered one of the most important factors in favor of breast feeding. Breast feeding is recommended in the low socio-economic groups where the likelihood of successful artificial feeding is often jeopardized.[4,5,8] The above statements are generally well accepted by the majority of physicians.

In the pediatric literature of a few years ago[14,15] statements that breast-fed infants thrive better than the artificially fed infants during the first months after birth are found frequently. Modern medical literature does not include a discussion of the problem because objective data are lacking to establish differences in relation to subsequent growth and development between breast and artificially fed infants.[5] The purpose of this study is to present data on the growth in height and weight of a selected small group of breast-fed infants.

Growth data on breast-fed infants are difficult to find in the literature. Holt's data[16] in 1897 were the earliest in the American literature. The average weights from his weight

TABLE 1B

BREAST-FED BOYS; WEIGHT IN POUNDS

	Birth	1 mo.	2 mo.	3 mo.	4 mo.	5 mo.	6 mo.	7 mo.
	8.9	10.0	11.6	13.2	14.4	15.2	15.9	16.6
	6.7	9.1	11.7	13.3	14.7	15.6		
	6.9	9.5	11.8	13.3	14.7	15.6	16.5	
	6.9	8.9	11.9	13.7	14.9	16.1	17.0	
	6.2	8.7	11.1	13.1	14.8	15.5	16.4	
	7.3	8.5	10.2	12.3	13.9	15.2	16.2	
	7.7	8.9	10.9	12.0	12.4	13.2		
			11.6	13.4	14.9	16.1	16.8	18.0
	6.6	9.2	10.7	12.3	13.8	15.1	15.9	
	7.8	10.1	12.3	14.1	15.3	15.8		
	9.4	11.5	13.6	14.9	15.6	16.3	17.6	
	7.1	9.1	11.3	13.4	14.9	16.1	16.8	17.4
	6.6	9.0	12.5	14.7	16.5	17.8	19.1	20.4
	6.2	8.1	11.0	12.0	15.4	16.4	18.1	
	7.3	10.3	12.8	14.5	16.3	17.0	18.5	19.0
	7.3	10.4	11.5	13.8	15.3	16.0	17.6	
	8.2	10.4	12.7	15.9	17.2	17.3	18.4	
	7.8	11.8	14.1	15.9	17.1	19.0	20.3	
	7.0	8.1	9.5	12.0	12.7	15.0		
	8.6	11.1	12.6	14.0	15.6	18.6		
	7.5	10.7	12.5	14.7	15.5	16.3		
N	20	20	21	21	21	21	15	5
Md	7.3	9.3	11.7	13.4	14.9	16.1	17.0	18.0
16%	6.6	8.54	10.77	12.3	13.13	15.13	15.9	
84%	8.12	10.64	12.70	14.75	16.19	17.24	18.48	

curve for breast-fed infants are plotted in the growth curve (graph 1). This curve was made from complete weight charts of 100 healthy nursing infants and the incomplete charts of about 300 others. Although the curve was apparently constructed without regard to the sex of the infants, there is the statement that girls throughout the year are on the average 0.23 kg. lighter than the boys. It is further stated that the weight curve for properly, artificially fed infants does not differ from that of breast-fed infants, except in the slower gain of the first 1 or 2 months, although this difference is usually made up before the sixth month is reached.

Koplik[14] recorded average weight for breast-fed and artificially fed infants as shown also on graph 1. The average birth weight was 3.4 kg. The number of infants and their sexes are not given. The type or types of formula fed to the artificially fed group also is not stated.

Faber and Sutton[15] reported on a small sample of breast-fed and artificially fed infants. They concluded that during the first three months after birth breast-fed infants showed a significantly better mean weight gain than bottle-fed infants; that later artificially fed infants gain more rapidly and this superiority becomes progressively greater up to the time of weaning. In the Faber-Sutton group supplemental feeding was introduced in the infant's diet much later than currently accepted standards.

Hou and Su and Liang (quoted by Albanese[17]), reporting on the growth of Chinese

TABLE 2A

BREAST-FED GIRLS; HEIGHT IN INCHES

	Birth	1 mo.	2 mo.	3 mo.	4 mo.	5 mo.	6 mo.	7 mo.
	19.2	22.3	23.6	24.8	25.7	26.5	27.4	28.3
	19.1	20.9	23.0	24.1	24.9	25.8	26.3	
	19.1	21.2	22.5	23.7	24.6	25.6		
	19.7	20.3	21.9	23.8	24.5	25.1		
	17.3	18.8	20.6	21.9	22.9	24.1		
	18.1	21.0	22.4	24.0	25.2	25.7	26.4	
	21.6	23.1	24.4	25.2	25.9	26.6		
	21.5	22.3	23.5	24.4	25.1	25.8		
		21.4	22.7	23.8	24.7	25.5		
	19.1	21.5	22.8	23.7	24.7	26.1	26.6	27.2
	17.7	20.9	21.8	23.3	24.8	25.8		
	20.5	21.0	22.0	23.5	24.0	25.0	26.0	26.5
		22.2	23.5	24.0	25.5	26.7	26.7	27.5
		22.5	23.2	24.0	25.5	25.7	26.7	
		20.2	21.5	23.2	24.2	25.7	26.2	27.0
	20.0	21.7	22.2	23.7	24.5	25.2		
	17.0	22.5	24.0	24.2	25.2	26.0	26.2	27.5
		22.2	24.1	24.7	25.2	25.5		
	19.2	21.7	22.5	24.5	25.2	25.7	26.2	27.1
	19.7	21.2	22.7	23.5	24.2	25.0		
	20.5	22.2	23.2	24.5	24.7	25.2	26.0	26.5
	19.7	21.2	23.2	24.2	25.2	26.7		
		21.5	22.2	23.2	24.7	25.0	25.7	
	18.5	21.0	22.0	23.0	24.5	25.0		
N	18	24	24	24	24	24	13	8
M	19.31	21.47	22.74	23.85	24.80	25.61	26.29	26.55
S.D.	1.53	.95	1.26	1.15	.68	.68	.44	

infants under different nutritional environments, revealed an early and later nutritional failure in the first year after birth. Some of their data were on entirely breast-fed infants. Albanese explained the slower growth of the Chinese infants as compared with the present American standards by the poorer nutritional status of the Chinese mothers, by the racial characteristics and by the fact that these infants were not given supplemental foods.

Meredith[18] reviewed the American literature from 1850 through 1941 that give data on height during the first two years after birth. His conclusions after analyzing the data relevant to the present discussions were: 1. Infants fed pasteurized or evaporated cow's milk beginning at ages under 1 month are no shorter in average height at 3 months of age than infants receiving human milk. 2. Gain in average height between 3 and 6 months of age is not appreciably different for infants fed human milk than for those given evaporated or pasteurized milk.

Meredith, quoted by Boyd[19] in a recent publication, found that with the passage of time the average height and weight of groups of children of similar ancestry and economic status have increased significantly and that the increase is not limited to one race, one economic level, or one age period of childhood. Further, the increase in height and weight has taken place during a period that has been characterized by progressive lower-

TABLE 2B

BREAST-FED GIRLS; WEIGHT IN POUNDS

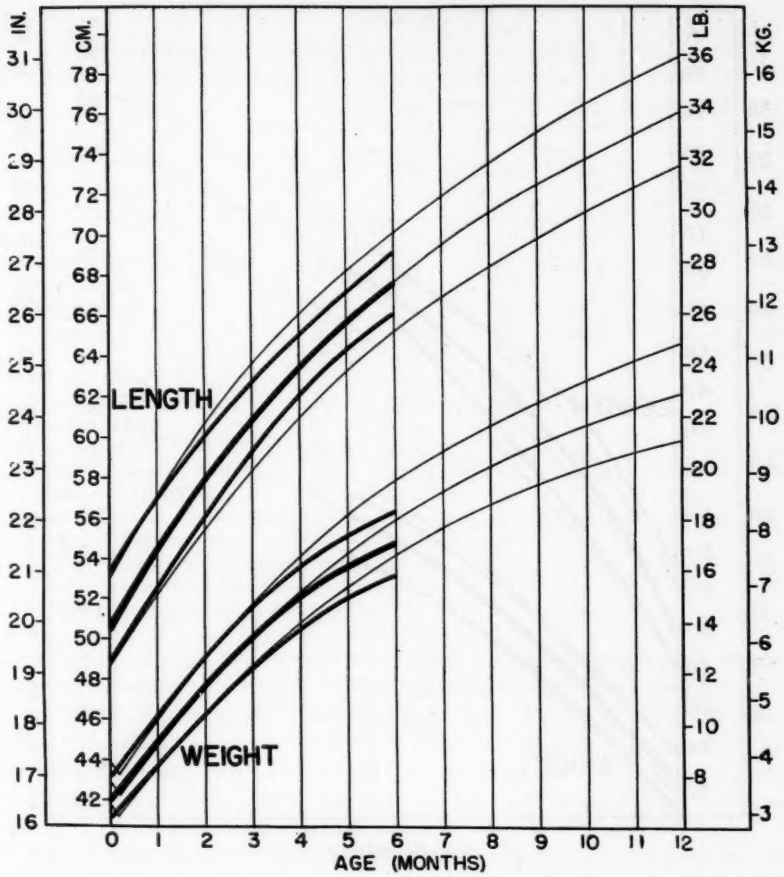
	Birth	1 mo.	2 mo.	3 mo.	4 mo.	5 mo.	6 mo.	7 mo.
	9.2	10.3	12.2	14.1	15.9	17.7	18.7	19.7
	7.5	9.1	11.1	13.2	15.1	16.5	17.7	
	7.3	8.5	10.0	11.6	13.1	14.7		
	7.3	9.2	11.9	13.3	14.6	15.3	16.0	
	4.7	6.4	9.3	11.7	13.6	14.7		
	6.6	9.3	11.4	12.9	14.2	15.9	17.6	
	10.3	11.0	11.9	13.1	14.5	15.6		
	9.4	10.6	11.7	12.8	13.6	14.4		
	6.7	8.9	11.3	13.2	14.4	15.6		
	8.3	9.9	12.5	14.6	16.1	16.6	17.4	18.0
	6.6	8.0	10.1	12.3	14.6	16.7		
	7.4	8.8	10.4	11.4	12.8	15.4	15.8	16.0
	8.1	11.1	12.7	14.1	15.2	17.1	17.3	18.2
	7.7	10.2	11.5	12.4	13.6	14.3	14.9	
	5.0	7.5	9.7	13.3	14.5	16.9	17.9	
	8.8	12.0	11.5	13.3	14.8	16.4		18.9
	6.4	9.8	11.1	12.2	13.5	15.1	16.0	
	7.8	11.7	13.1	15.0	16.4	16.9		18.3
	6.4	9.7	10.8	13.2	14.1	15.6	16.5	
	7.4	8.6	10.5	11.5	12.8	14.0		17.5
	8.9	9.8	11.6	13.2	14.2	15.4	16.0	
	8.3	8.2	10.7	12.2	13.8	17.0		17.0
	7.1	8.9	10.0	10.7	12.0	12.8	14.6	
	5.5	8.5	10.2	12.0	13.5	15.2		
Md	7.4	9.25	11.2	13.0	14.2	15.55	16.5	18.2
N	24	24	24	24	24	24	13	8
16%	6.10	8.10	10.00	11.58	13.00	14.36	14.97	16.12
84%	8.80	10.64	11.93	13.38	15.11	16.90	17.69	18.82

ing of the infant mortality rate, by lengthening of life expectancy, by decline in the incidence of many infectious diseases, and by development and application of the science of nutrition.

MATERIAL

The weight and height of a group of 21 male and 24 female, well infants from Iowa City were obtained at monthly intervals from birth to 6 to 7 mo. of age. The families of these infants were of better-than-average income and intelligence; the mothers were well fed during both pregnancy and lactation. All the infants in the group were fed entirely on human milk with the addition of supplemental feeding consisting of vitamin D 400 u., ascorbic acid 15 to 50 mg. derived from orange juice and started during the 1st 2 wk. after birth; at 3 mo. the introduction of 1 egg yolk as a soft custard, at 4 mo., 2 to 3 oz. of sieved fruits daily; at 6 to 7 mo. a fortified cereal product, not more than 2 oz. of ready-to-serve material; sieved meat was also used to replace either egg yolk or some of the vegetables or both 2 to 3 times a week. All infants were considered in good health throughout the period of observation except for occasional minor illnesses in a few of the infants, with negligible, if any, effect on growth. The height and weight of the infants were obtained without clothing by experienced personnel.

The infants, subjects of this study, were seen in the period from 1947 to 1951 in the Well Baby Clinic, Department of Pediatrics, University of Iowa Hospitals. The number of infants entirely breast fed was small in comparison with the total number of infants seen in the clinic in the same period of time. Infants who were partially breast fed were not included.



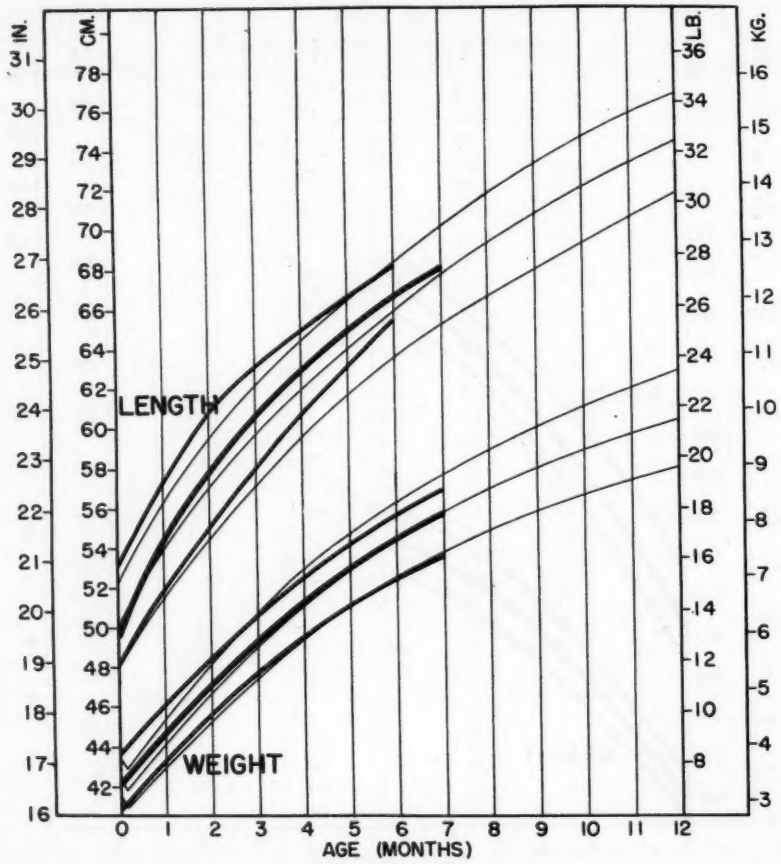
GRAPH 2. Growth curves of breast-fed male infants are shown in heavy lines. Light lines show standard Iowa growth curves[20] based on data from babies preponderantly artificially fed.

RESULTS AND CONCLUSIONS

The individual height and weight and respectively the mean and median values for each group of infants are tabulated in tables 1 and 2. Plotted on the standard growth charts[20] are the mean values plus and minus the standard deviation for height and the median values with the 16th and 84th percentile for weight (graphs 2 and 3).

The growth curve obtained by plotting the mean values for height and the median values for weight* from the above measurements showed insignificant variations from the average (middle curve) of the standard growth charts, except for a slight decline of the weight curve for the male infants in the fifth and sixth months. The significant findings led to the conclusion that the growth pattern of the group of breast-fed infants studied did not differ essentially from that of artificially fed infants.

* Mean values are used for height because there is a normal distribution for age group. Median (50th percentile) is used for weight because it is slightly skewed for age groups.



GRAPH 3. Growth curves of breast-fed female infants are shown in heavy lines. Light lines show standard Iowa growth curves[20] based on data from babies preponderantly artificially fed.

Recently[21] the growth pattern of a group of infants entirely artificially fed, of comparable size to the group of breast-fed infants here presented, was reported and compared with the Iowa standard growth curves. The authors found that the mean of both height and weight of the group was slightly above the corresponding values in the standard growth curves under consideration.

Another conclusion that can be drawn from the data obtained is that the growth charts at present in use in the Pediatric Service may be applied to breast-fed as well as to artificially fed infants.

It is difficult to evaluate the significance of the decline of the weight curve of the male infant group in the fifth and sixth months with the small number of infants studied. The analysis of the individual weights of the male infants in that period showed that the deceleration of weight gain was not due to a growth failure of a few of the infants, but was due to a gain in weight at a slower rate for most of the infants. It is hoped that addi-

TABLE 3

AVERAGE HEIGHT AND GAIN IN AVERAGE HEIGHT (CM.) FOR BREAST-FED INFANTS

	Average				Increment	
	3 mo.		6 mo.		birth to 3 mo.	3 to 6 mo.
	cases	av.	cases	av.	(cm.)	
MALES						
*Benedict and Talbot (1921)	13	60.8	12	67.3		6.5
Meredith (1941)	5	60.7			10.4	
†Francis (1940)	25	60.3	25	66.7		6.4
‡present data (1951)	21	60.3	15	66.6	10.5	6.3
BOTH SEXES						
*Benedict and Talbot (1921)	26	60.3	24	65.7		5.4
Meredith (1941)	9	60.3			10.1	
†Francis (1940)	50	59.8	50	66.2		6.4
§Bakwin and Bakwin (1931)	—	59.4	—	67.5		8.1
‡present data (1951)	45	59.9	28	66.2	10.5	6.3

* Group "mostly breast-fed."
† Group entirely or largely breast-fed for 3 mo. or more.
‡ Only group entirely breast-fed up to 6 mo.
§ Group "partially or completely breast-fed."

tional data from a larger number of subjects may be obtained to determine whether the pattern of growth is consistent for the male infants breast-fed as above described.

As can be seen in graph 1, both groups of breast-fed babies previously mentioned (Holt's and Koplik's) gained weight at a slower rate than the Iowa standards, and the artificially fed group (Koplik's) did not gain weight as fast as the breast-fed groups.

The growth of the breast-fed infants of the Hou and Su and Liang[17] group was decidedly inferior to the group herewith reported.

Table 3 gives Meredith's data[18] (height), those collected from the literature, and the present author's values.

DISCUSSION

The known nutritional requirements of the full term infant in the first few months after birth will be met when infants are either successfully breast- or artificially fed, provided that adequate supplemental feeding is given at the proper time in each case.[4,9] Theoretically, according to what is known regarding the nutritional needs of the growing infant, the artificially fed infant receives up to four times more calcium than the breast-fed infant and if he gets the usual amounts of vitamin D, he often retains more calcium than the breast-fed babies ingest and, therefore, might be expected to have a faster skeletal growth and thus a slight edge in height over the breast-fed infant.[9]

Other requirements for a satisfactory feeding of infants are absence of harmful bacteria and easy digestibility.[4] Artificial feeding of today has been perfected to meet well these requirements.[4,7,8]

From the present studies it is concluded that the pattern of growth of breast-fed infants does not differ significantly from that of the artificially fed infants of the same

socio-economic group. The advantages of human milk, stated earlier in this paper, are not altered by the findings of this study. Breast feeding is desirable for most normal infants and should be encouraged and preferred. However, modern artificial feeding is an adequate substitute for breast feeding when the latter is not practical or feasible.

Summary

The data of measurements of 21 male and 24 female breast-fed infants from birth to 6 to 7 months of age are presented. The infants were born of well fed mothers, coming from families of better than average income and intelligence.

The pattern of growth of these infants is compared with that of a larger group, the majority of whom were artificially fed infants of the same socio-economic status.

It is concluded that the pattern of growth of the breast-fed infants does not differ significantly from that of artificially fed infants of the same socio-economic group.

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SPANISH ABSTRACT

Patrones de Crecimiento de Grupos Seleccionados de Lactantes Alimentados al Seno en la ciudad de Iowa

En la literatura pediátrica de hace pocos años no era raro encontrar afirmaciones diciendo que los lactantes alimentados al seno se desarrollan mejor que los alimentados artificialmente durante los primeros meses de la vida. La literatura moderna declina discutir el problema por la falta de datos objectivos que establezcan diferencias en relación al crecimiento y desarrollo subsecuente entre lactantes alimentados al seno y artificialmente. El objeto de este estudio es presentar datos acerca del crecimiento de un grupo pequeño seleccionado de 21 niños y 24 niños de la ciudad de Iowa en quienes se registró el peso y la estatura mensualmente desde el nacimiento hasta la edad de siete meses. Las madres de estos niños estuvieron bien alimentadas y sus familias eran de inteligencia y medios económicos mejores que el promedio.

El patrón de crecimiento de estos lactantes se comparó con el de un grupo mas grande de lactantes, la gran mayoría de ellos alimentados artificialmente, de las mismas condiciones sociales y económicas.

De dicha comparación se concluyó que el patrón de crecimiento de los lactantes alimentados al seno no difiere significativamente del de los alimentados artificialmente del mismo grupo socio económico.

Las ventajas de la leche humana, como su esterilidad, facil disponibilidad, indices de mortalidad y morbilidad mas bajos en los lactantes alimentados con ella, y la satisfacción emocional que madre e hijo obtienen hacen que su uso sea deseable para la mayoría de los niños normales y debe estimularse y preferirse. Sin embargo, es importante señalar que la alimentación artificial moderna la substituye adecuadamente cuando aquella no es practica o factible.

State University of Iowa

ON THE NATURAL REGRESSION OF PULMONARY CYSTS DURING EARLY INFANCY

By JOHN CAFFEY, M.D.
New York City

PULMONARY air cysts in infants and children develop through a variety of mechanisms—congenital anomaly;[1,2] check-valvular bronchial obstruction;[3,4] pulmonary necrosis (bacterial and fungal); echinococcosis; and trauma.[5] When cysts are demonstrated roentgenographically in the lungs of infants younger than six months, they are commonly attributed to congenital anomalies and are removed surgically[6–10] in the belief that they are naturally irreversible.

The purpose of this paper is to point out that spontaneous regression without surgical removal is the rule for pulmonary cysts even where they are demonstrated during the first weeks and months of life. The author's experience shows that, if excision is postponed, almost all these early pulmonary cysts disappear spontaneously after periods of several weeks or months. Even if a cyst persists, as it will occasionally do, the patient usually thrives. The cases of Vollmer[11,12] and of Potts and Riker[10] are of interest in this regard. In a girl 6 years of age Vollmer demonstrated a pulmonary cyst with an air-fluid level; when she was re-examined roentgenographically at 27 years of age a cyst was found in the same site. During the intervening 21 years, the patient had led an active healthy life and had been free of respiratory infections. In the case of Potts and Riker, a pulmonary cyst was shown roentgenographically in an infant 5 weeks of age; surgical excision was advised and refused. At 6½ years, this cyst was still visible radiologically although the child had thrived and had not suffered from an excessive number or from excessively severe respiratory infections.

The present author's experience indicates that all patients should be watched for long periods in the hope that complete spontaneous regression will occur. The only exception to this policy is the rare case of acute respiratory obstruction due to sudden and marked expansion of the cysts; in such a case surgical excision is urgent and appears to be a life-saving measure. The evaluation of hazards to life under such circumstances should, in the author's opinion, be left to the judgment of pediatricians rather than surgeons, because pediatricians are more familiar with the frequency, during the first months of life, of violent symptoms which are actually transient and benign in the very young, but which might indicate surgical intervention in older patients. It should also be emphasized that it is impossible to differentiate congenital irreversible cysts which need to be treated surgically from acquired naturally reversible cysts, on roentgenographic grounds; and that in most cases the congenital or acquired origin of the cysts cannot be determined with certainty from the microscopic findings.

This paper reports prolonged clinical and roentgen studies in 13 cases in which cystic roentgen changes were demonstrated before the sixth month of life. The first eight cases

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From the Department of Pediatrics, College of Physicians and Surgeons, Columbia University and Babies Hospital, New York City.

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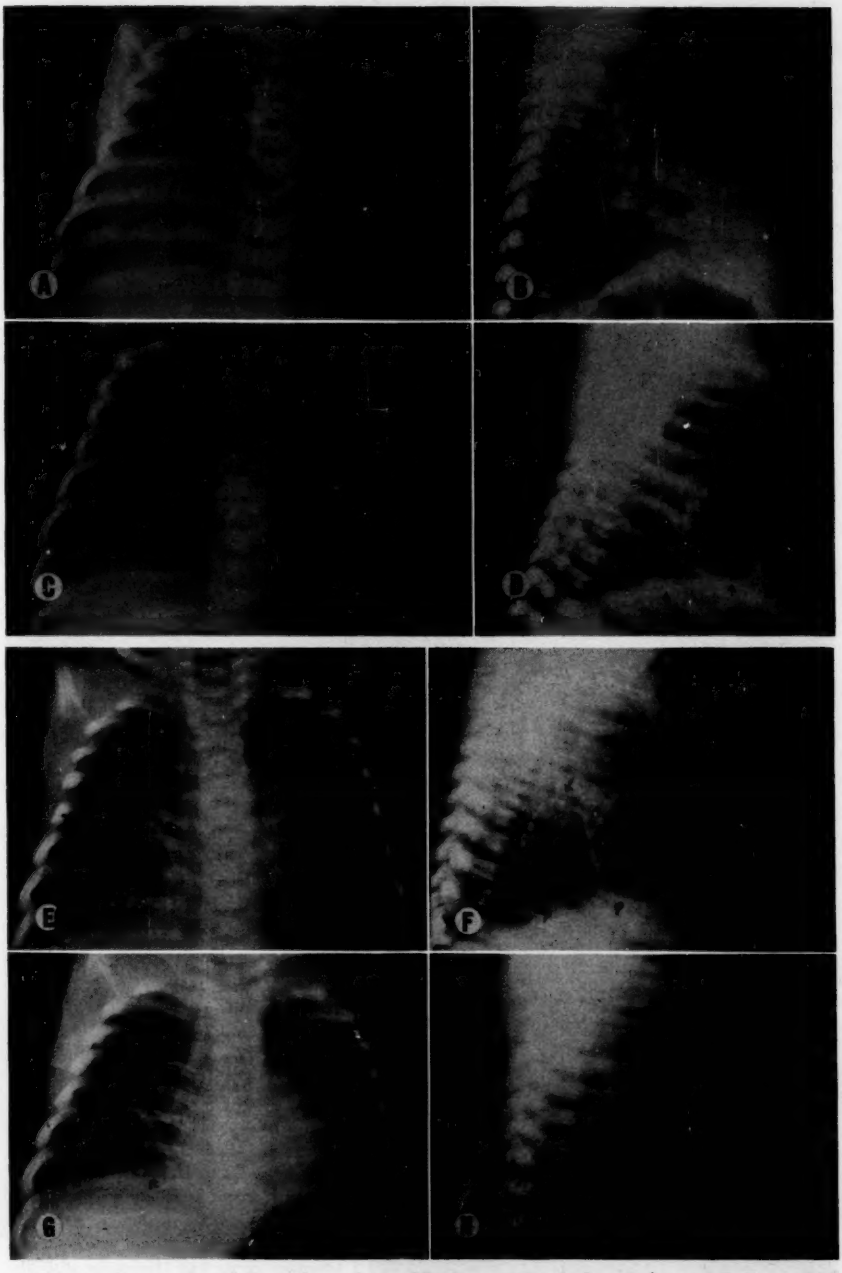

FIG. 1. Case 1. A and B: 7 days of age. Massive opaque shadow in base of R lung which suggests infected congenital fluid cyst or pneumonic consolidation. C and D: 15 days of age. Three large air cavities with well defined walls in site occupied previously by massive opaque shadow. E and F: 26 days of age. Cavities are larger than on 15th day. G and H: 43 days of age. Single large cavity is still visible.

represent a variety of pulmonary cysts which disappear completely. Cases 9 and 10 are examples of loculated pyopneumothorax which, in some stages of the disease, simulates pulmonary cystic disease very closely. In Cases 11 and 12, massive obstructive emphysema was demonstrated without evidence of cavitation in the lungs or a cyst wall; these cases are included because this type of pulmonary disease often needs surgical interference.[13,14]

Cases

Case 1, K. J., a female Negro, was transferred from the obstetric nursery at 6 days of age because of fever and lethargy which began at 4 days of age. Physical findings in the chest were normal but roentgen examination disclosed a large opaque segment in R lung which suggested pneumonic con-

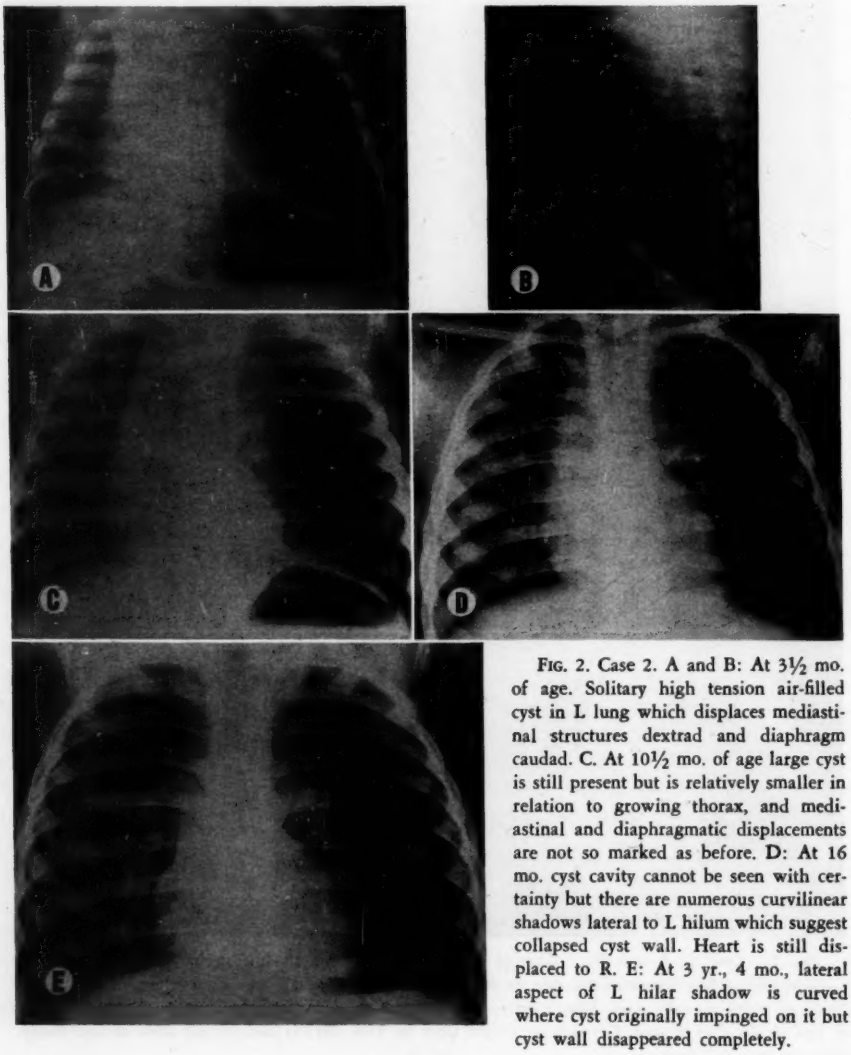

Fig. 2. Case 2. A and B: At 3½ mo. of age. Solitary high tension air-filled cyst in L lung which displaces mediastinal structures dextrad and diaphragm caudad. C. At 10½ mo. of age large cyst is still present but is relatively smaller in relation to growing thorax, and mediastinal and diaphragmatic displacements are not so marked as before. D: At 16 mo. cyst cavity cannot be seen with certainty but there are numerous curvilinear shadows lateral to L hilum which suggest collapsed cyst wall. Heart is still displaced to R. E: At 3 yr., 4 mo., lateral aspect of L hilar shadow is curved where cyst originally impinged on it but cyst wall disappeared completely.

solidation in R middle and lower lobes (Figs. 1A and B). Fever and lethargy disappeared after a few days of combined treatment with penicillin and streptomycin. At 15 days of age (Figs. 1C and D), after she had been asymptomatic for 4 days, 3 large cavities were found in the base of R lung, in the site previously occupied by consolidation. At 20 days, these cavities were distinctly larger (Figs. 1E and F). By 43rd day of age a single large cavity was still visible in the position of R middle lobe (Figs. 1G and H). On 75th day there was some irregularity in density in the base of R lung but no cavities could be seen. On 102nd day, this cavity had disappeared completely. In later films, made on 160th day and not shown here, findings in thorax were normal.

During this period of observation, infant grew and developed normally. She had a second respiratory infection during 3rd month with cough and noisy breathing, from which she recovered without treatment.

This is an example of lobar pneumonia which developed on 4th day of life, followed by triple air cyst formation identified on 15th day of life with gradual spontaneous regression of cysts which had disappeared completely by 102nd day.

Case 2, E. K., was first seen at 3½ mo. of age with history of labored breathing since birth. Excepting dyspnea, patient had been asymptomatic. He had thrived and had been free of upper respiratory infections. Chest was deep ventro-dorsally and heart was displaced to R. Roentgen examination disclosed a large thin-walled cavity which occupied most of L hemithorax (Figs. 2A and B). Cavity was aspirated but its size and shape were not modified after removal of large amounts of gas, which indicated free flow of gas from bronchial tree into the cyst. At this time congenital cystic disease of lung or acquired tension loculated emphysema seemed the most likely diagnosis. Surgical excision of cyst was advised by some consultants.

It was decided to observe the infant, in hope that the cyst would disappear spontaneously, and he has now been under observation for 3 yr., 4 mo. Dyspnea has gradually disappeared with advancing age and he has thrived at all times. He has not been subject to frequent or severe respiratory infections. Films made during the 10th months (Fig. 2C) showed persistence of large single air cyst with dextral displacement of mediastinal structures. At 16 mo. (Fig. 2D) cyst had disappeared spontaneously but curvilinear shadows lateral to hilum suggested collapsed cyst wall and the heart was still displaced dextrad. At 2 yr., 3 mo., heart was still displaced slightly to R; but at 3 yr., 4 mo. (Fig. 2E), thorax was normal roentgenographically.

At no time was this patient in difficulty from respiratory obstruction or respiratory infection. He grew and developed normally notwithstanding presence of the large tension cyst and displacement of mediastinum.

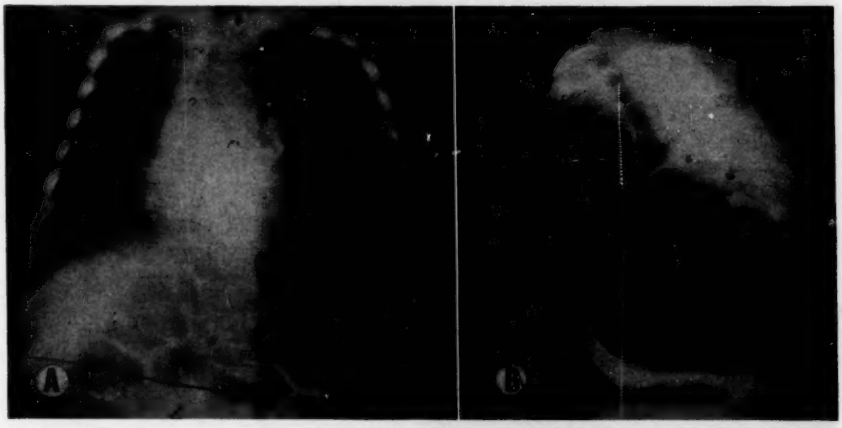

FIG. 3. Case 3. A and B: Frontal and L lateral projections at 5 mo. of age, 2 days after onset of fever, cough, dyspnea and cyanosis. Two large tension cysts in L lung with distinct walls. Dorsal segment of diaphragm is displaced far caudad. Only slight dextral displacement of mediastinal structures. Upper part of L lung projects dextrad well beyond R side of spine; heart and great vessels are displaced dorsad by overdistended L lung.

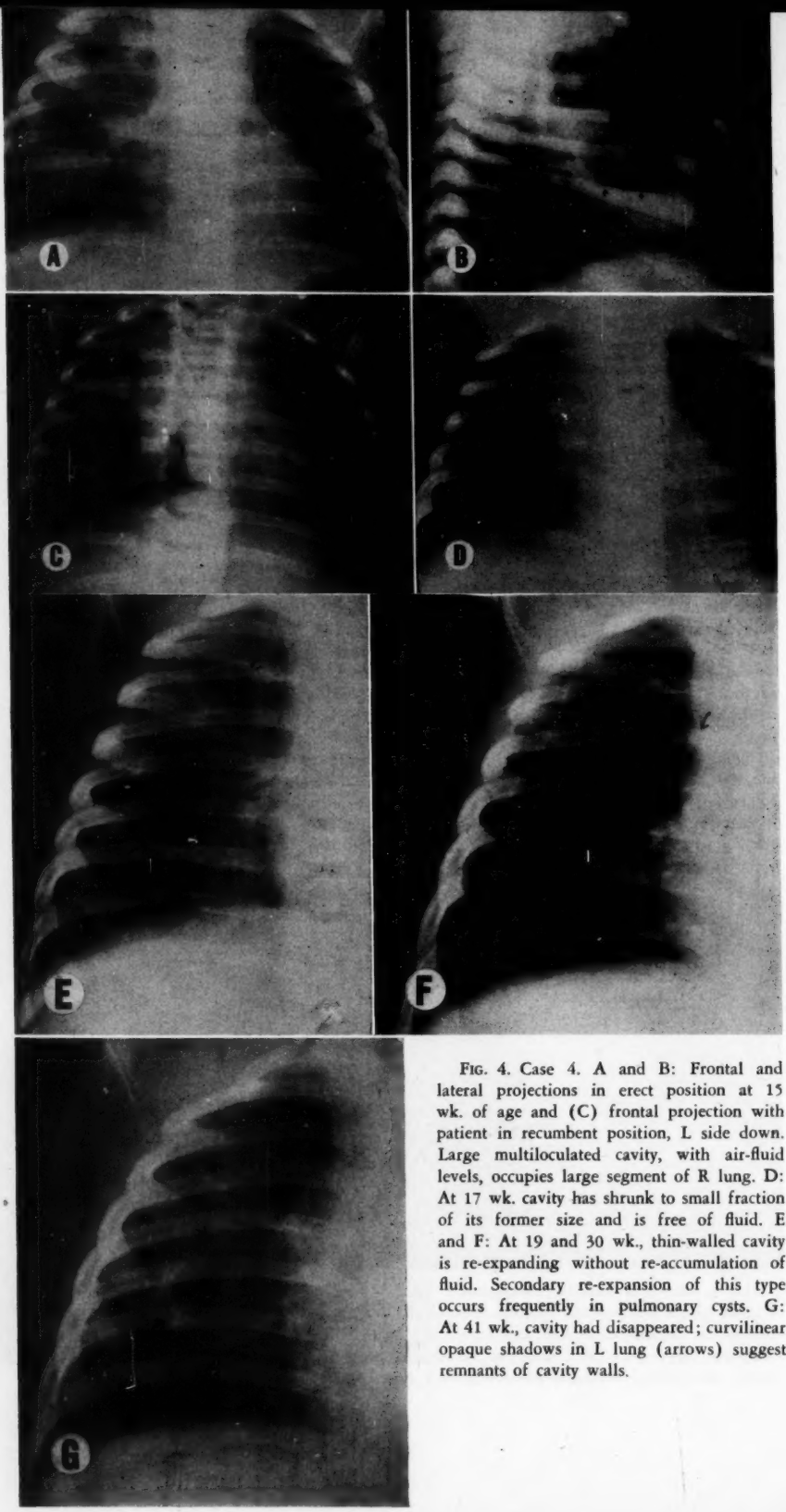

FIG. 4. Case 4. A and B: Frontal and lateral projections in erect position at 15 wk. of age and (C) frontal projection with patient in recumbent position, L side down. Large multiloculated cavity, with air-fluid levels, occupies large segment of R lung. D: At 17 wk. cavity has shrunk to small fraction of its former size and is free of fluid. E and F: At 19 and 30 wk., thin-walled cavity is re-expanding without re-accumulation of fluid. Secondary re-expansion of this type occurs frequently in pulmonary cysts. G: At 41 wk., cavity had disappeared; curvilinear opaque shadows in L lung (arrows) suggest remnants of cavity walls.

This is an example of a large solitary tension cyst, identified at 3½ mo., which disappeared between 10th and 16th mo.

Case 3, G. P., had had frequent upper respiratory infections since birth but had thrived until 5th mo. when he was admitted after 2 days of fever, cough and dyspnea which had been getting progressively worse since onset. At admission he exhibited cyanosis, labored breathing and a constant short hacking cough. Left side of thorax was hyper-resonant, enlarged, practically immobile, and breath sounds could not be heard. Heart was displaced to R. Roentgen examination disclosed 2 enormous radiolucent, air-filled cavities in L hemithorax limited by relatively thin ring shadows of increased density (Figs. 3A and B). Dorsal segment of L leaf of diaphragm was displaced far caudad. Heart and other mediastinal structures in contrast were in normal position. Upper portion of L lung extended dextrad well beyond R side of spine. Barium given by mouth showed that esophagus was in normal position and there was no evidence of a diaphragmatic hernia. Aspiration of 300 and 600 cc. gas from lower cavity caused no improvement in dyspnea, and no diminution in size of cyst or its displacement of the diaphragm. Oxygen content of gas aspirated from cyst approximated that of alveolar air.

At surgical consultation, early but not immediate excision of cysts was advised. During 24 days of hospital residence, cyanosis, fever and cough persisted but they were less pronounced than at admission. Roentgen findings in chest remained unchanged. Parents then took infant from the hospital against advice when the large tension cavities were still present.

Seventeen months later, when he was 22 mo. of age, he was examined again; physical findings and roentgen findings in his chest were normal. Mother stated that all symptoms had suddenly disappeared a few days after he left the hospital, following first admission, and that he had been in good health thereafter. His physician reported he was well and thriving at 46 mo. of age.

This is an example of sudden spontaneous regression of 2 high tension cysts with severe clinical symptoms and a stormy clinical course of about 6 wk.

Case 4, J. R., was well until 3 mo. of age when she developed a respiratory infection with cough and fever. Two weeks later these symptoms were still present and dullness was detected in upper half of R hemithorax but breath sounds were normal without rales. Films at 15 wk. showed a large multilocated cavity, filled with air and fluid, in upper part of R lung (Figs. 4A, B and C). Low grade fever and cough persisted for about 1 wk., after which appetite gradually improved and patient thrived. She was followed at home by her pediatrician during next 2 yr. and was always healthy, without abnormal physical signs in lungs. In serial films the cavity gradually shrank, redilated and then disappeared completely at 53 wk. (Figs. 4D, E, F and G).

This is an example of complete regression of a large multiloculated cavity which contained considerable fluid with air during early phase of disease.

There were 4 additional similar cases of cystic disease in lungs with spontaneous regression while the patients were thriving.

Case 5, R. D., showed normal findings in thorax in films made at 4 days of age. On 14th day a large opaque segment containing a small cavity was demonstrated. On 28th day several radiolucent small cavities with well defined walls occupied the site of earlier opaque lesion. On 48th day most of the opacity had disappeared and small cavities had coalesced into a single large cavity. Patient was asymptomatic and left the hospital without later examinations. Lesions in this case were following the identical benign course of those described in earlier cases, but regression was incomplete at last examination.

Case 6, M. B. was well until 23 days of age when a respiratory infection with facial cellulitis and fever developed. On 32nd day, films of chest disclosed irregular consolidation in both lungs with numerous large and small cavities in both lungs; one cavity in base of L lung measured 5 cm. in its longest diameter. On 37th day, much of the patchy consolidation had cleared but cavities persisted and had increased in size. On 42nd day, the opaque consolidation had disappeared completely but 2 large cavities, one in base of each lung, persisted. On 49th day, lungs were normal roentgenographically and patient was healthy and gaining weight. In a follow-up on 310th day, lungs were normal clinically and roentgenographically. Patient suffered orginally from staphylococcal bacteremia with pneumonia, maxillary cellulitis, facial cellulitis and meningitis.

Case 7, D. D., was admitted at 10 days of age with complaints of jaundice and anemia since 2nd day. At the other hospital mother was found to be Rh-negative with a high blocking antibody and baby B, Rh-positive. Despite replacement transfusion of 300 cc. followed by 2 conventional trans-

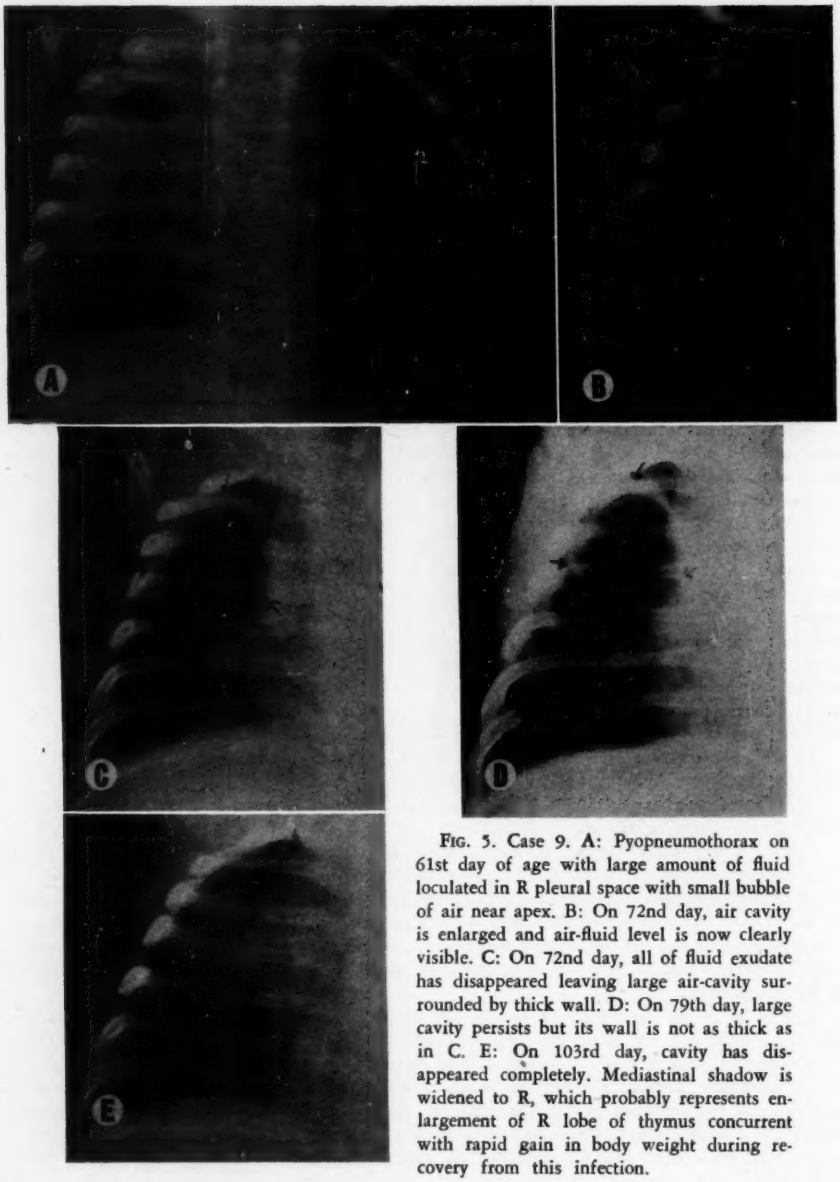

FIG. 5. Case 9. A: Pyopneumothorax on 61st day of age with large amount of fluid loculated in R pleural space with small bubble of air near apex. B: On 72nd day, air cavity is enlarged and air-fluid level is now clearly visible. C: On 72nd day, all of fluid exudate has disappeared leaving large air-cavity surrounded by thick wall. D: On 79th day, large cavity persists but its wall is not as thick as in C. E: On 103rd day, cavity has disappeared completely. Mediastinal shadow is widened to R, which probably represents enlargement of R lobe of thymus concurrent with rapid gain in body weight during recovery from this infection.

fusions of 50 cc. each of blood, infant's hemoglobin continued to drop. Jaundice had disappeared by 10th day. On 13th day he was doing well and the blood was normal after transfusion of 50 cc. whole blood. On 14th day a slight fever of 38.0°C. developed. This continued irregularly until 22nd day with high ESR (52 to 111 mm. in 1 hr.) when a film of thorax revealed a large opaque shadow, in which there was a small radiolucent shadow suggestive of cavitation, in R lung. On 26th day the radiolucent shadow was large and there was a short air-fluid level. On 30th day the opaque shadow of consolidation was clearing but the shadow of cavity was increasing. On 34th day the cavity was larger and surrounded by a thick wall. On 38th day this wall was much thinner. On 44th day, the cavity was greatly enlarged, limited by a wall of paper thinness, and occupying now most of region which had been occupied originally by the large shadow of increased density. On 59th day cavity had diminished slightly in size and its wall was less distinct. On 87th day, the large cavity had disappeared completely. Lungs were normal roentgenographically and patient was thriving.

Case 8, E. N., weighed 2450 gm. at birth and was well until 11 days of age when she became febrile, lethargic and cyanotic. In films made on 11th day, a large segment of R lung was opaque. In serial films on 13th, 15th, 18th and 24th days, the large opaque shadow persisted unchanged. On 28th day, radiolucent multiple small cavities were found in the opaque region and 4 days later, on 32nd day, the small cavities had coalesced into a single large cavity with disappearance of all of opaque elements. On 52nd day, lungs were normal roentgenographically. This patient was treated from the onset with sulfadiazine and penicillin and was asymptomatic after 14th day.

Case 9, K. G. was irritable on the 52nd day of life and developed fever 2 days later. She was treated with penicillin for acute pharyngitis and otitis media. Fever continued without cough for 4 days when stools became frequent and loose. At this time there were no conclusive physical findings in chest. Roentgen examination on 61st day showed a large opaque shadow in R hemithorax, which suggested perilobar loculation of pleural exudate around R upper lobe, which contained a small radiolucent shadow near its top, suggestive of a cavity (Fig. 5A). Thick yellow pus was aspirated from site of the opaque shadow, from which grew staphylococcus aureus, mannitol and coagulase positive. Penicillin and chloramphenicol were started and fever subsided after 3 days. Serial films (Figs. 5B, C, D and E) show gradual decrease in the opaque shadows with gradual increase in size of cavity and then its final disappearance. Patient thrived during period of evolution and then involution of cavity.

This is an example of loculated pyopneumothorax which simulated a single, large infected congenital cyst and which finally disappeared completely without surgical treatment.

Case 10, V. L. During the 7th wk. of life, fever developed and roentgen examination at another hospital showed entire right hemithorax to be opaque. After treatment with penicillin, fever subsided but roentgen changes in thorax persisted. When first examined by the author at 11 wk. of age, R side of chest was dull to percussion; in films of thorax, upper three-quarters of R hemithorax was obscured by a massive opaque shadow which suggested perilobar loculation of pleural exudate around R upper lobe and which contained a large bubble of air, near its top (Fig. 6A). Aspiration in site of the opaque shadow yielded 25 cc. creamy yellow pus which contained Staph. aureus hemolyticus, mannitol and coagulase positive. Patient remained afebrile throughout his hospital residence.

In follow-up observations during more than 3 yr. he was healthy and grew and developed normally. During 1st 6 mo. of life, air in the loculated pleural exudate gradually increased as the exudate gradually decreased (Figs. 6B, C and D). With advancing age the multiple smaller cavities (Fig. 6B and C) coalesced into a single large cavity. In films at 31 and 37 mo., all signs of cavitation had disappeared, but there were still poorly defined shadows of increased density which suggested residual changes in pleura and possibly in R lung. This patient was observed carefully by thoracic surgeons, who feared irreversible congenital cystic disease of lung; they wisely postponed and then abandoned surgical treatment in view of the favorable clinical course and gradual roentgen involution of roentgen changes.

This is an example of loculated pyopneumothorax which simulated multiple congenital cystic disease early, and then later a single large congenital cyst, and which finally disappeared completely.

The author has seen 3 other examples, not shown here, of loculated pyopneumothorax during first weeks of life which exhibited cavities, in films, which resembled infected congenital cystic disease of lung, all of which disappeared spontaneously without surgical treatment. In one, a large

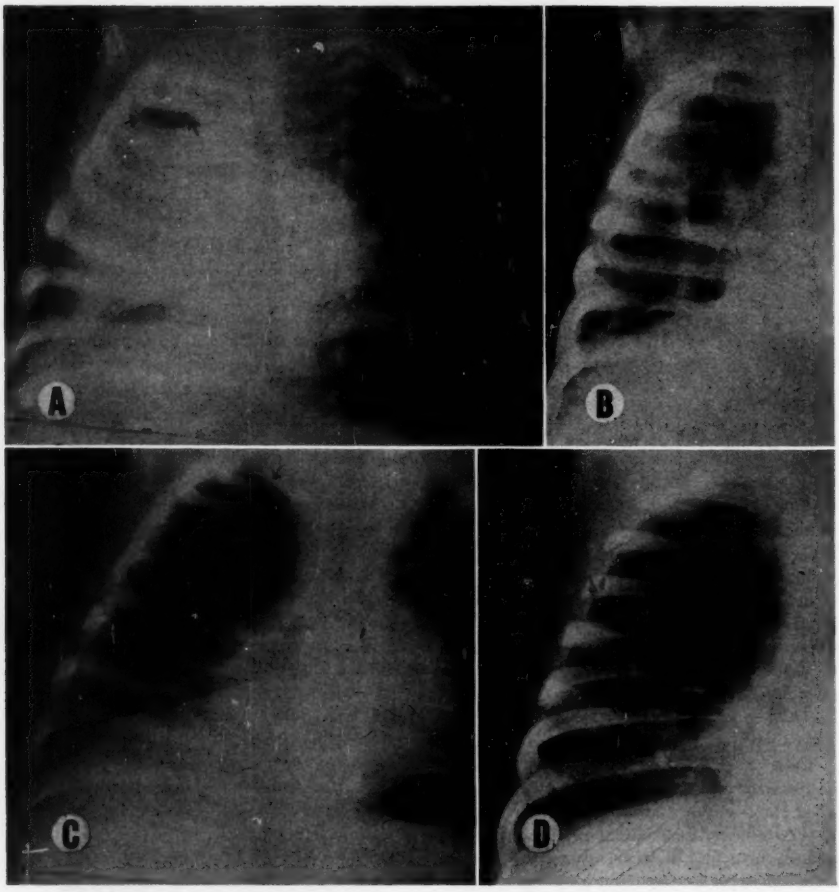

FIG. 6. Case 10. A: At 11 wk. of age, pyopneumothorax loculated around R upper lobe with small air bubble (arrows) in large amount of pus. Apparent shift of mediastinal structures to R is due to rotation of patient. B: At 12 wk., there are numerous smaller cavities in greatly reduced pleural exudate. C: At 16 wk., loculated air has now coalesced into 2 or 3 layer cavities and little pleural exudate remains. D: At 26 wk., loculated air is now collected in single large cavity and there is no fluid pleural exudate.

cavity with limiting ring shadow was demonstrated on 36th day of life; in a second, multiple small ringed cavities were found during 6th wk. of life; and in a third case, a single large cavity was present during 4th mo. of life and multiple small cavities during the 5th mo.

Case 11, F. F. was normal at birth. Heavy breathing was first noted during 5th wk. of life; there were no signs of infection at the time of onset or prior to onset. Dyspnea persisted, and during 9th week overaeration and distension of R lung was demonstrated roentgenographically (Figs. 7A and B). At this time patient was observed in the hospital for 1 wk. The only clinical signs were high-pitched expiratory crow with frequent dry cough. Respiratory rate varied between 40 and 60/min. There was no cyanosis. He has now been observed for 24 mo. with serial physical and roentgen examinations. Dyspnea and stridor gradually disappeared and crow could not be detected after 6th mo. With advancing age and growth, overdistension of R lung gradually diminished both absolutely

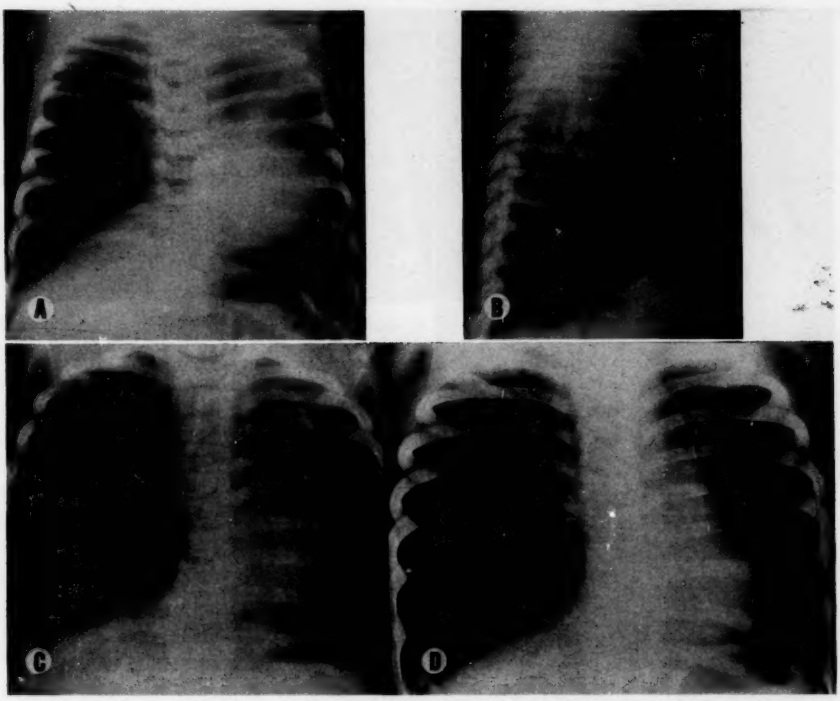

FIG. 7. Case 11. Frontal and lateral projections of thorax during 9th wk. Right lung is overdistended, R leaf of diaphragm is driven caudad and mediastinal structures are displaced to L—almost to L lateral thoracic wall. In lateral projection, dilated lung in front of heart and great vessels has displaced them dorsad. There is no evidence of air-cyst formation in dilated R lung. In C and D, at 12th and 28th mo., respectively, R lung is still overdistended, with exception of apex, but mediastinal structures have shifted mediad and R leaf of diaphragm has shifted cephalad to almost normal position. At 28th mo. (D) mediastinal shadow is compressed in R side but L mediastinal border is in normal position. Left lung is now normally visible. At fluoroscopy respiratory movements were almost normal; on R there was only slight decrease in diaphragmatic movement.

and in relation to the thoracic volume (Figs. 7C and D). At 26 mo. of age patient was a robust vigorous child of normal size with good nutrition. He had had a normal number of transient respiratory infections from which he always made rapid complete recoveries. Longstanding overdistension of R lung did not interfere with nutrition, development or growth and he had no episodes of acute respiratory obstruction.

This is an example of extreme lobar emphysema during first weeks of life, without air-cyst formation, which showed gradual but incomplete improvement during 1st 2 yr. while the infant thrived.

Case 12, A. K., began to breath with difficulty during the 5th wk. of life and a few days later began to cough. There were no signs of respiratory infection at time of onset. The only significant physical finding was right-sided displacement of heart. Roentgen examination at 51 days of age disclosed a large radiolucent segment in base of L lower lobe with dextrad displacement of heart and mediastinum (Fig. 8A). After 4 days in hospital all symptoms disappeared and patient has now been observed for 40 mo. He had thrived at home with only occasional respiratory infections from which he recovered completely and rapidly. In serial roentgen examinations, of which only 2 are reproduced here, hyperaeration of basilar segment of L lower lobe persisted but was relatively and

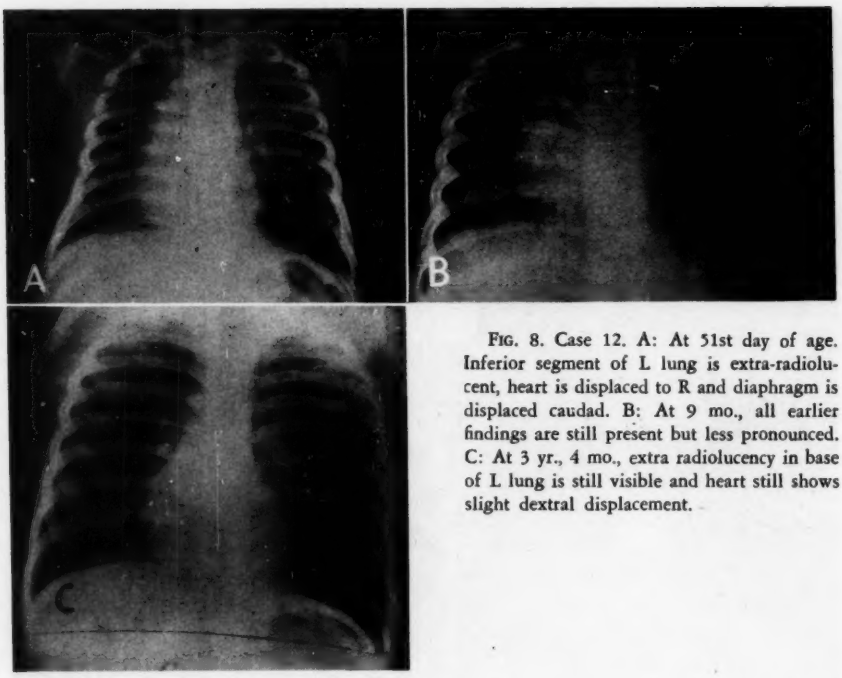

FIG. 8. Case 12. A: At 51st day of age. Inferior segment of L lung is extra-radiolucent, heart is displaced to R and diaphragm is displaced caudad. B: At 9 mo., all earlier findings are still present but less pronounced. C: At 3 yr., 4 mo., extra radiolucency in base of L lung is still visible and heart still shows slight dextral displacement.

absolutely greatly diminished (Figs. 8B and C), in comparison with findings at onset during 5th wk. of life.

This is an example of persistent segmental emphysema of L lung, from 51st day of life to 40th mo., with progressive slow improvement of emphysema while the patient flourished.

The author has seen 2 other patients, in whom massive lobar emphysema was identified before the 6th mo. of life, who were treated by surgical excision, because attending physicians and surgeons believed that the pulmonary lesion offered a serious threat to the life of the patient. In one, R middle and R lower lobes were removed at 4 mo. of age after 3 mo. of dyspnea; patient recovered quickly and has thrived since, and now at 40 mo. of age is healthy in all respects. In the excised pulmonary specimen, a large cavity, not visible in roentgenograms, was found which was lined with ciliated columnar epithelium. In the other case, acute dyspnea and paroxysmal cyanosis developed at 2 mo. of age. Massive obstructive emphysema of L lung was shown in film and fluoroscopic examination. Clinically patient's condition seemed to be critical and after 3 days of observation the entire L lung and thymus were removed surgically. In excised lung, the alveoli were widely expanded but no epithelialized cavities were found. No cause for obstruction was identified, either at surgical exploration or in the excised specimen. This patient has grown and developed normally and at 3½ yr. of age is a strong lively boy. Left side of chest is smaller than R side, and lower part of sternum is depressed but spine is straight. In the roentgen examination at 3½ yr. the smaller L hemithorax is opaque and contains all of the mediastinal structures; L leaf of diaphragm is high. Right lung and R hemithorax are dilated and R leaf of diaphragm is depressed with a wide amplitude of excursion.

COMMENT

Thirteen cases of infants younger than 6 months of age are recorded; large air-cysts developed in the lungs, in 8 cases, and in the pleural spaces in 5 cases. In all of them, the cysts regressed without surgical treatment. In the youngest patient, triple large cavi-

ties were present on the 15th day of life and had replaced pneumonic consolidation which had been visualized on the seventh day of life. During prolonged periods of observation, these infants grew and developed normally, and they did not suffer unduly from respiratory infections. When last examined all of them were in good health and free of respiratory symptoms.

Five examples of large air-cysts are described, two in detail (Cases 9 and 10), in which the air appeared to be trapped in the pleural space during the course of pleural infections. The similarity of the roentgen findings in these cases of located pyopneumothorax to the findings in intrapulmonary air-cysts demonstrates the great difficulty of differentiating these two lesions on roentgen grounds. It is possible that in some cases of multiple cysts, some of the cavernous lesions were in the pleural space and some in the lungs, simultaneously in the same patient. It is also probable that all the air originally loculated inside the lung may occasionally leak through defects in the pleura into the pleural space and become loculated there, secondarily. The possibility of pleural exudate associated with a pulmonary air-cyst but without air in the pleural space, must also be kept in mind in the evaluation of the roentgen changes.

In four cases of massive pulmonary emphysema without visible cyst formation, lobectomy was found necessary in one and pneumonectomy in a second case. These two were the only patients treated surgically in the entire group. In the author's experience, massive emphysema without cyst formation has been a more serious lesion than the cysts themselves.

When air cysts are demonstrated roentgenographically in the lungs of very young infants, neither the immediate nor the ultimate prognosis can be established with certainty. There are no clinical or roentgen features which warrant an opinion concerning the prenatal or postnatal origin of the cysts. Thickness of the cyst wall is an unreliable index because both thick and thin walls have been found in both congenital and acquired cysts and in individual cysts, thickness of the wall varies at different times. Both kinds of cysts may contain shifting air-fluid levels. Even after thoracotomy, the true nature of the cyst and its prognosis cannot be estimated accurately. The decision for surgical interference must be based on knowledge of the natural course of many cysts determined by prolonged clinical and roentgen studies. In the studies of 13 such patients, not treated surgically, spontaneous regression occurred in all 13.

The concept that cystic disease of the lung is commonly congenital prevails today largely because of the frequency with which the diagnosis of congenital cystic disease is made by pathologists on specimens removed surgically or at necropsy. These anatomic diagnoses are generally accepted without question by clinicians who approve surgical excision of the cysts because anatomic diagnoses so frequently imply that a naturally irreversible lesion has been removed. Clinical experience, on the other hand, with cysts which are not removed surgically teaches that almost all the cysts demonstrated radiologically disappear spontaneously.[3–5] It is obvious that either congenital cysts are naturally reversible or the criteria for the histologic diagnosis of their prenatal origin are not valid.

The accuracy of the microscopic evaluation of the pathogenesis of pulmonary cysts merits careful scrutiny. The high incidence of cysts during infancy and early childhood does not ensure their prenatal development. If these cysts do evolve prior to birth, they should be encountered with approximately the same frequency in fetuses and newborns as they are in older infants and children. Such is not the case.

Actually the number of authentic cases of prenatal and neonatal cysts is surprisingly small.[1,2,5] Potter,[15] in her large experience with fetal lungs, has found only two examples of fetal cystic disease, and in one of these cases the findings were not conclusive. During the last 22 years at the Babies Hospital in New York City, cystic disease has been found in a single stillborn infant; none has been found in neonates. The author has recently completed a radiologic study of 5000 unselected newborn infants delivered at the Sloane Hospital; in not a single case were there roentgen changes in the lungs suggestive of cystic disease. Films were made on the 1st, 2nd or 3rd days of life.

Surprisingly few malformations of the lungs or of other structures have been found in association with cysts of the lungs to support the hypothesis of their congenital origin. Dickson[16] reports that "other anomalies have been found in connection with cysts of the lung but this appears to be certainly uncommon." Ravitch and Hardy[9] point out that supplemental lobes and anomalous vessels are found so commonly without cysts, that these anomalies should not be considered causative factors when they are found with cysts.

The microscopic diagnosis of congenital cytic disease depends principally on the presence of an epithelial lining made up of columnar ciliated or low cuboidal cells, on the internal face of the cyst wall. The presence or absence of this epithelial lining cannot be detected radiologically, and one can only speculate as to the microscopic nature of the cyst walls which regress spontaneously. The high incidence of epithelial linings in the removed cysts suggests, however, that many of the cysts which disappear spontaneously are also covered with epithelium. There are several reasons for not accepting an epithelial lining of the cyst wall as conclusive proof of its prenatal origin. Respiratory epithelium, like epithelium in other parts of the body (skin, gastrointestinal tract), tends to cover acquired defects after injury, by proliferation. Epithelial linings in known acquired cysts have been frequently observed. Maier[17] states that acquired pulmonary cavities may be lined by cuboidal, columnar or metaplastic squamous epithelium; he also mentions the epithelization of tuberculous cavities. Pryce[18] found that abscess cavities in the lung sometimes become lined with ciliated epithelium. Sellors and coworkers[19] described pulmonary cavernous spaces lined by ciliated columnar epithelium; the acquired nature of these lesions is indisputable because they were observed to have developed in segments of the lungs which, originally, were normal radiologically.

The velocity of proliferation of human bronchial epithelium after injury is not known; especially in the very young. In an experimental study on the tracheal epithelium of young adult rats, Condon [20] found the first signs of epithelial regeneration as early as 4 to 6 hours after tracheotomy; 8 to 10 hours after the injury the regenerated epithelium had respiratory characteristics. In some animals, flat stratified epithelium covered the tracheal defects completely and individual cells were already ciliated, 24 hours after tracheotomy. By the end of the third day, in most animals, the entire defect was fully epithelized. In all cases, 3 to 10 days after tracheal incision, the early squamous epithelium had reverted to columnar ciliated epithelium. If the bronchial epithelium of human infants proliferates at similar or greater velocities, and it may well be that repair of respiratory epithelium is more rapid in a human newborn than in an adult rat, the presence of epithelial linings in pulmonary cysts is indeed a spurious index of the prenatal origin of the cyst, even when they are found in the youngest infants.

Some investigators have used absence of carbon pigment in neighboring parts of the lung as evidence of the prenatal origin of pulmonary cysts. Koontz[21] emphasizes that cysts are found at all ages and states it would be difficult to determine whether the lesion was

congenital or acquired were it not for the total lack of pigment in congenital lesions, which shows that the affected part of the lung had never functioned and therefore the cyst antedated birth. Conway[5] takes the stand that absence of carbon pigmentation in the parenchyma in some cases of cystic disease is not conclusive evidence of its prenatal development but rather implies that the cyst was formed during early infancy and merely impeded the respiratory function of the parts lacking in pigment. Dickson[16] concludes that the presence or absence of carbon pigment in the parenchyma is not always a reliable feature for the differentiation of congenital from acquired cysts. During the first weeks and months of life there is little or no pigment in the lungs so that absence of pigment in very young patients is not significant.

The presence in the cyst wall of such elements as cartilage, smooth muscle, elastic tissue and mucous glands has also been used as conclusive evidence of the prenatal origin of the cyst. These bronchial elements in a cyst wall can be reasonably explained by the purely mechanical factors of bronchial dilatation beyond bronchial obstruction. It is highly probable that the bronchi beyond check-valvular bronchial obstruction dilate as well as the alveoli, and with continuing high intrabronchial pressure and progressive

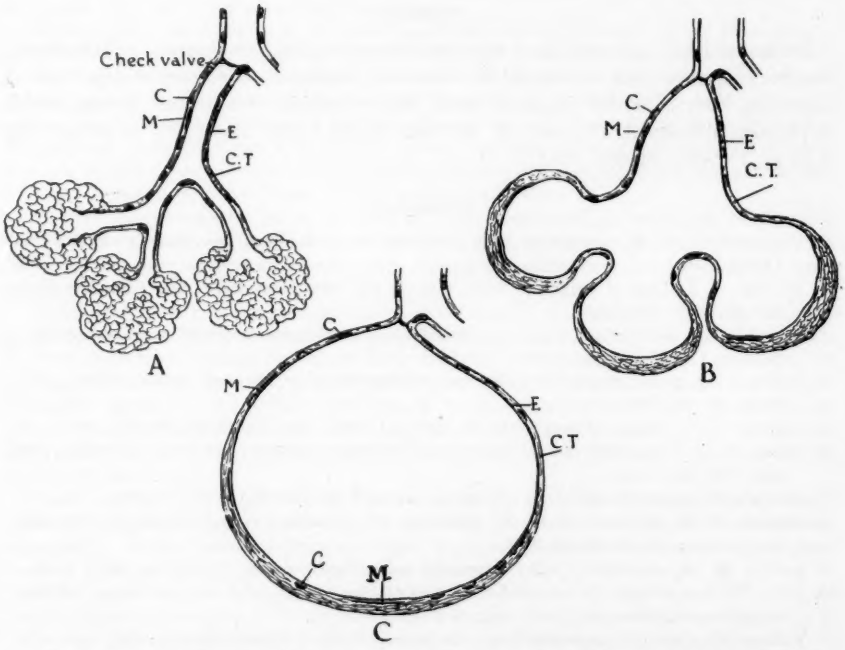

FIG. 9. Schematic representation of progressive incorporation of elements from bronchial walls into wall of acquired pulmonary cyst, forming beyond check-valvular bronchial obstruction. In A, first stage, alveoli are beginning to dilate but bronchi are not affected. In B, later stage, all of tributary bronchi beyond obstruction are distended and their walls are being displaced outward toward periphery of cyst. In C, cyst is fully dilated into roughly spherical shape; cartilaginous and muscular components, originally in bronchial walls, are now scattered in different parts of cyst wall; owing to simple progressive distension of bronchi. (C, bronchial cartilage; M, bronchial muscle; E, bronchial epithelium; C. T., connective tissue.)

bronchial distension and elongation, the bronchial walls themselves are incorporated into the cyst wall, as depicted schematically in figure 9. Stretching of the bronchi would scatter the bronchial elements such as cartilage and muscle irregularly in the cyst wall. At the same time the bronchial epithelial layer would be stretched and finally torn by rapid stretching and its fragments separated as distension continued. The inner surface of the cyst would be partially covered with patches of bronchial epithelium. Extension of the epithelium by proliferation from these numerous and scattered foci could cover the entire surface of the cyst with a complete epithelial lining in a relatively short time. In the author's opinion, the presence of bronchial elements in the cyst wall and an epithelial lining on its internal face are by no means certain evidence of prenatal development because all these histologic features can be satisfactorily explained by postnatal acquired mechanisms.

Conclusions

The immediate and ultimate prognosis of pulmonary and pleural cysts, untreated surgically, is excellent, even during the early weeks of life.

Addenda

Fischer and his colleagues have reported obstructive lobar emphysema in five infants, due to congenital deficiencies in the bronchial cartilages, and compressing vascular anomalies, both of which produced check value bronchial obstructions, beyond which emphysema developed. (Fischer, H. W., and others, Lobar emphysema in infants and children, J. Pediat. **41**:403, 1952.)

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SPANISH ABSTRACT

La Regresión Natural de los Quistes Pulmonares Durante la Primera Infancia

El propósito de este artículo es señalar que la regla en la evolución de los quistes del pulmón es su regresión espontánea sin extirpación quirúrgica aún cuando hayan sido demostrados durante las primeras semanas y meses de la vida.

Los quistes pulmonares aéreos del lactante y del niño se desarrollan por varios mecanismos: malformación congénita, obstrucción bronquial por sistema de válvula, necrosis pulmonar (bacteriana y micósica), equinococosis y trauma.

Cuando los quistes se demuestran roentgenológicamente en los pulmones de lactantes menores de 6 meses, generalmente se atribuyen a una malformación congénita y se les extirpa quirúrgicamente por la creencia de que son de naturaleza irreversible.

El autor publica las historias de 13 casos con estudios clínicos y de rayos X por largo tiempo, en los cuales los quistes se demostraron roentgenológicamente antes del sexto mes de la vida. Ocho de estos enfermos representan una variedad de quistes pulmonares que desaparecen por completo; dos casos son ejemplos de píoneumotórax loculado, los cuales, en algunos estadíos de la enfermedad simulan muy de cerca una enfermedad quística pulmonar; dos casos con enfisema obstructivo masivo sin cavitación en los pulmones o quiste de la pared y se incluyen en la serie porque a menudo requieren cirugía y finalmente dos casos de enfisema lobar masivo que fueron tratados por excisión quirúrgica porque se creyó que existía una seria amenaza de la vida.

En todos los enfermos los quistes desaparecieron espontáneamente sin extirpación quirúrgica, y durante largos períodos de observación, los pacientes crecieron y se desarrollaron normalmente no sufriendo infecciones respiratorias indebidamente. Cuando se examinaron por última vez todos estaban sanos y sin síntomas respiratorios.

La similitud de los hallazgos roentgenológicos en los casos de píoneumotórax loculados con los de quistes aéreos intrapulmonares demuestra la gran dificultad para diferenciar ambas lesiones por rayos X. Varias posibilidades pueden suceder; en quistes múltiples unos pueden estar en el pulmón otros en el espacio pleural, o bien el aire originalmente loculado en el pulmón puede escapar por defectos pleurales al espacio pleural y locularse en él secundariamente y, finalmente, es posible que un exudado pleural se asocie a un quiste pulmonar aéreo pero sin aire en el espacio pleural. En cinco de los casos había grandes quistes aéreos y el aire parecía estar atrapado en el espacio pleural durante la evolución de una infección pleural.

Desde el punto de vista clínico y roentgenológico no existe característica alguna que autorice a opinar acerca del origen pre o postnatal de los quistes. El grosor de la pared quística no es decisivo, pues pueden hallarse paredes gruesas o delgadas en quistes congénitos o adquiridos, y el grosor varía en diferentes épocas y ambas variedades pueden contener niveles hidroaéreos.

Si en la actualidad prevalece el concepto de que la enfermedad quística del pulmón es comunmente congénita, es en gran parte por la frecuencia con que los patólogos hacen el diagnóstico de enfermedad quística congénita en especímenes extirpados quirúrgicamente o de la necropsia.

Estos diagnósticos anatómicos son en general aceptados sin objeción por los clínicos quienes aprueban la excisión quirúrgica de los quistes por que los diagnósticos anatómicos muy frecuentemente implican que una lesión de naturaleza irreversible ha sido extirpada, pero si la experiencia clínica demuestra que casi todos los quistes demostrados radiológicamente desaparecen en forma espontánea, es obvio que, o bien los quistes congénitos son reversibles en forma natural o no es válido el criterio seguido para hacer el diagnóstico histológico de su origen congénito o prenatal.

El autor hace una serie de consideraciones a este respecto. Clínicamente, la gran frecuencia de los quistes durante la primera infancia no asegura su desarrollo prenatal pues si así sucediera debían

ser tan frecuentes en fetos y recién nacidos como en lactantes y niños y tal no es la realidad, pues de hecho, el número de casos auténticos de quistes pre o neonatales es sorprendentemente pequeño.

Potter, con su gran experiencia en pulmones fetales solo ha encontrado un caso definitivo de enfermedad quística fetal y otro dudoso.

En el Babies Hospital de la ciudad de Nueva York se ha encontrado un solo caso en 22 años. En un estudio radiológico realizado por el autor con 5000 recién nacidos no seleccionados, no se encontró un solo ejemplo de quistes del pulmón. Asímismo, son pocas las malformaciones pulmonares o de otras partes que se asocian a los quistes para poder sostener la hipótesis de su origen congénito.

Histopatológicamente, el diagnóstico de enfermedad quística congénita depende principalmente de la presencia en la cara interna de la pared quística de un epitelio de revestimiento formado por células ciliadas arregladas en columnas o células cuboidales bajas. Sin embargo, hay varias razones para no aceptar este criterio, primeramente, el epitelio respiratorio como cualquiera de otras partes del cuerpo, tiene tendencia a cubrir por proliferación los defectos adquiridos consecutivos a su lesión y efectivamente se ha observado epitelio de revestimiento en quistes adquiridos, en cavernas tuberculosas y abscesos cavitarios. Por otra parte, aunque no se sabe cual sea la velocidad de proliferación del epitelio bronquial humano después de una lesión, si en el recién nacido ésta es igual o bien mayor que la encontrada en ratas adultas, la presencia de epitelio de revestimiento en los quistes pulmonares es en realidad un índice falso del origen prenatal de un quiste, aún cuando se trate de los lactantes mas pequeños.

Algunos investigadores han tomado la ausencia de pigmentación por carbón en las áreas vecinas del quiste como prueba de su origen prenatal infiriendo que la parte afectada del pulmón nunca ha funcionado y por consiguiente antecede al nacimiento, pero también puede interpretarse el hecho diciendo que el quiste se formó tempranamente durante la infancia y que impidió la función respiratoria de las partes con ausencia de pigmento y en realidad durante las primeras semanas y aun meses de la vida hay muy poco o nada de pigmento en los pulmones, de manera que su ausencia en enfermos muy pequeños no tiene significación.

Finalmente, también se ha usado como prueba concluyente del origen prenatal de un quiste la presencia en sus paredes de elementos tales como cartílago, músculo liso, tejido elástico y glándulas mucosas, pero estas estructuras pueden explicarse muy probablemente por la dilatación simultanea tanto de los alveolos como del segmento bronquial distal al sitio de obstrucción de tipo valvular y a medida que dicha dilatación bronquial progresa las paredes bronquiales se incorporan a la pared del quiste y finalmente se distribuyen en forma irregular, tejidos como músculo y cartílago de origen bronquial cubríendose posteriormente de epitelio, por la proliferación de los restos de epitelio brónquial, que termina por tapizar la superficie entera de la cara interna del quiste. Por consiguiente, tampoco la presencia de elementos bronquiales en la pared del quiste es una prueba cierta de su desarrollo prenatal.

El autor concluye que segun su experiencia todos los enfermos con quistes pulmonares deben vigilarse por largos períodos con la esperanza de que ocurra una regresión espontánea completa y la única excepción a este principio son los casos raros de obstrucción respiratoria aguda debida a una expansión súbita y marcada del quiste, en cuyo caso la extirpación quirúrgica es urgente y parece ser un procedimiento para salvar la vida. La evaluación de los peligros para la vida bajo tales circunstancias en opinión del autor, deben dejarse a juicio del pediatra mas bien que del cirujano, porque aquél está mas familiarizado con la frecuencia, durante los primeros meses de la vida, de síntomas violentos que son efectivamente transitorios y benignos en el lactante, pero que en pacientes más grandes podrían considerarse como casos quirúrgicos. El autor también enfatiza que es imposible diferenciar radiológicamente los quistes congénitos irreversibles que deben tratarse quirúrgicamente de los quistes adquiridos de naturaleza reversible y que en la mayor parte de los casos, el origen congénito o adquirido de un quiste no puede ser determinado con certeza por sus caracteres microscópicos.

622 West 168th Street

RENAL WATER REQUIREMENT OF INFANTS FED EVAPORATED MILK WITH AND WITHOUT ADDED CARBOHYDRATE

By EDWARD L. PRATT, M.D., AND SELMA E. SNYDERMAN, M.D.
New York City

THE present day trend in the continuing evolution of infant feeding is towards simplification of food mixtures, particularly the tendency to omit supplementary carbohydrate and to use a single mixture throughout infancy.[1] However, in addition to providing appropriate nutrients, one should consider the stresses that the prescribed mixture may impose on other physiologic functions.

Unmodified cow's milk could be expected to impose an increased renal solute load on the kidney. The present study was designed to evaluate this quantitatively; that is, to determine to what extent the margin of safety against dehydration is decreased when added carbohydrate is omitted from the milk mixture. In this study, the renal load imposed by a mixture of evaporated milk, water and added carbohydrate is contrasted in the same infants with the renal solute load from feedings of only evaporated milk and water, each mixture being fed at the same caloric level. Having determined the two average renal solute loads the authors have calculated the obligatory urinary water requirements for any concentration of the urine and have also determined the urinary concentration which must be achieved for each renal load when the amount of water available has been diminished by increased extrarenal losses or lowered water intake. Thus renal load, which is related to the type of diet, has real practical significance for the doctor attempting to provide proper water balance for the infant.

METHODS

Six male premature infants, aged 10 to 30 days, weighing over 1800 gm., who were apparently healthy and gaining well, were utilized. It was hoped that premature infants under the conditions of the study would have relatively small and fairly uniform extrarenal electrolyte losses.

The modified milk mixture was a stock mixture composed of evaporated milk 100 cc., dextrimaltose without salt 14.2 gm. and water to make 220 cc. final volume. The unmodified milk mixture consisted of a stock mixture of evaporated milk 100 cc. plus water to make a final volume of 155 cc. Thus each mixture contained about 0.9 cal./cc. Appropriate amounts of each stock mixture were fed to provide the desired number of calories. The percentage distribution of calories and the average level of actual intake are given in table 1.

Each infant received both diets successively for two 6 day periods. Three infants had the modified mixture followed by the unmodified mixture and in the other 3 infants the order of feedings was reversed. During the last 48 hr. on each diet two 24 hr. urine specimens were collected. Total volume and freezing point depression of each sample were measured. A cryoscope with a Beckman thermometer was used to determine freezing points. Results for the 2 samples were averaged, except in one instance (Patient III), where one urine collection was believed to be incomplete.

Osmolar concentration of the urine was calculated by dividing freezing point in degrees Centi-

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From the Department of Pediatrics, New York University College of Medicine and the Children's Medical Service, Bellevue Hospital, New York City.

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TABLE 1

Mixture	Percentage Distribution of Total Calories			Actual Intake/kg./day	
	Protein	Carbohydrate	Fat	Cal.	Evap. Milk
Modified Milk	14.1%	49.5%	36.4%	133	66.6 cc.
Unmodified Milk	20.0%	28.5%	51.5%	131	93.3 cc.

grade by 1.86 and multiplying by 1000 to give moM/l.[2] Renal solute load was calculated by multiplying osmolar concentration of urine by its volume in liters. Body weights used in calculating values/kg. body weight were the averages of weights on days the urine specimens were collected.

RESULTS

Table 2 displays the results for each infant and also the average for all infants on the modified and unmodified milk mixtures.

The renal solute load while receiving the mixture with additional carbohydrate had a mean value of 19.7 mosM/kg. body weight/day with a standard deviation of 1.8 mosM/kg./day. The unmodified milk mixture resulted in a renal load of 36.4 ± 3.1 mosM/kg. body weight/day; a value 85% higher. The mean difference in renal solute

TABLE 2

TWENTY-FOUR HOUR URINE SPECIMENS

Patient	Age	Body Wt.	Diet	Urine Volume	Solute Concentration	Total Solutes	Total Solutes/ kg./day	Ratio of Solute Loads $\frac{Su}{Sm} \times 100$
	Days	gm.		cc./d.	mos^M/l.	mos^M/d.	mos^M/kg./d.	%
I_1	16	2325	Mod.	120	336	40.3	17.3	233
I_2	22	2320	Un.	135	694	93.7	40.3	
II_1	12	1840	Mod.	91	444	40.4	21.9	167
II_2	18	1990	Un.	114	637	72.6	36.5	
III_1	13	2000	Mod.	81	495	40.1	20.1	155
III_2	19	2010	Un.	85	737	62.6	31.1	
IV_1	11	1880	Un.	72	985	71.0	37.7	193
IV_2	17	2060	Mod.	92	436	40.1	19.5	
V_1	20	2020	Un.	84	845	71.0	35.1	188
V_2	26	2140	Mod.	78	514	40.1	18.7	
VI_1	23	2560	Un.	142	677	96.2	37.6	172
VI_2	29	2890	Mod.	214	295	63.2	21.8	
$A11_1$			Mod.				19.7	185
$A11_2$			Un.				36.4	

load produced by feeding the unmodified mixture as opposed to the modified mixture was 16.5 mosM/kg. body weight/day plus or minus the standard error of 1.63 mosM/kg./day. Hence, this increase is highly significant ($P<0.01$) statistically.[3]

Comment

The unmodified milk mixture resulted in an intake of about 40% more protein and minerals than the milk with added carbohydrate. As expected, the higher protein and higher mineral intake led to an increased renal solute load. In these small, rapidly growing infants the mean difference was an increase of 85%. Chart 1, which is derived from the relationship: urinary water requirement equals renal solute load divided by the concentration of the urine expressed in osmoles/liter, shows the obligatory renal water requirement/kilogram body weight/day versus urinary concentration for the solute loads from each diet. Thus the contrast in water expenditure by the kidneys for the two diets at any urinary concentration can be determined readily. If there were no over-all concentration of the urine so that the urine were at the same concentration as the plasma (about .310 osM/l.) the renal water requirements would be 64 and 117 ml./kg./day for the modified and unmodified milk mixtures respectively. Similarly, at a urinary concentration of 700 mosM/l., which is about the maximum concentration for newborn infants,[4] the urinary water required would be 28 and 52 cc./kg./day respectively. At maximal concentration of the urine for older infants[5] 16 and 30 cc. renal water would be needed. These relationships and the difference in renal water requirement on the two diets are apparent in chart 2.

The determination of the urinary concentration that would have to be achieved to re-

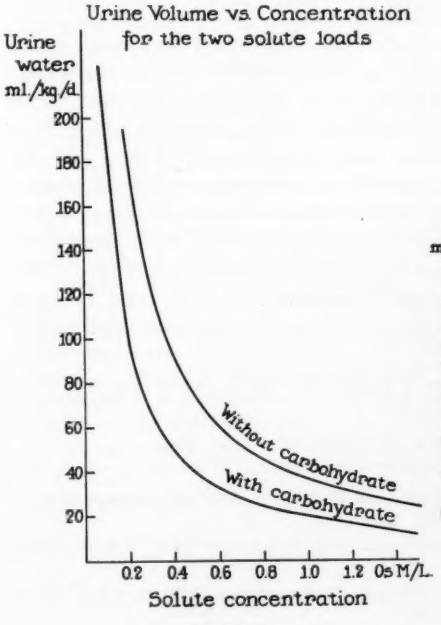

Chart 1

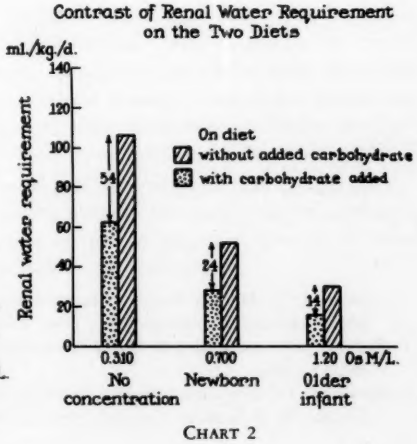

Chart 2

move the solute load imposed by each diet for any given amount of water available for excretion by the kidneys may be made by referring to chart 1. For example, if only 40 cc. water/kg. body weight were available for urine formation due to decreased water intake or because of increased extrarenal losses, such as from the gastrointestinal tract[6,7] or from the lungs and skin in hot weather,[7,8] then those infants receiving the modified milk would be required to concentrate the urine to only 490 mosM/l.; whereas, those fed the unmodified mixture would have to achieve 910 mosM/l., a concentration very likely beyond the ability of the kidneys of the newborn infant or any infant with renal impairment due to dehydration, shock or intrinsic renal disease.

Both milk mixtures considered here, if fed at the customary concentration of 20 cal./ounce (0.7 cal./ml.), provide, with the water of oxidation, a large amount of water to cover losses by all routes, about 190 cc./kg. Hence, it is only when the feeding is concentrated or abnormal extrarenal losses are present that the larger renal load imposed by the unmodified milk mixture may compromise the water balance and well being of the infant. Expressed another way, the larger renal load reduces the margin of safety in water balance for any given intake.

Clearly this study contrasts merely the physiologic stress on renal capacity, and thereby water balance, as produced by these two types of feedings and no attempt has been made to evaluate their nutritive values. Other studies[9,10] would seem to indicate their equality from this point of view.

It is of interest that Patient IV at the age of 11 and 12 days, weighing 1880 gm., achieved a urinary concentration of 980 and 990 mosM/l. on two consecutive days, possibly indicating that the concentrating power of the infants' kidneys matures quite rapidly.[11]

Summary

The renal water requirement of six rapidly growing small infants on a food mixture composed of solely evaporated milk and water has been compared with the renal water requirement in the same infants on isocaloric feedings of evaporated milk, added carbohydrate and water. The higher protein and mineral intake of the unmodified milk mixture resulted in an 85% increase in the renal solute load compared with the load from the modified mixture. Although this increase in renal load, and hence renal water requirement, may be of little significance under the usual conditions of water intake and expenditure, the margin of safety against dehydration has been decreased. At the same time, this larger renal solute load may be an important factor in compromising water balance and well being unless additional water is supplied whenever the usual intake is appreciably decreased, the extrarenal water expenditure is increased or there is impairment of the ability to produce a concentrated urine.

Thus the practical importance while planning infant feedings of considering properties in addition to purely nutritive factors is emphasized.

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SPANISH ABSTRACT

El Requerimiento Hídrico Renal en Lactantes Alimentados con Leche Evaporada con y sin Adición de Carbohidratos

La tendencia actual en la evolución continua de la alimentación del lactante va hacia la simplificación de las mezclas de alimentos, en particular a omitir la adición de carbohidratos suplementarios y usar una sola fórmula láctea durante toda la lactancia. Sin embargo, además de considerar la adición de substancias nutritivas apropiadas, se debe considerar la sobrecarga que la fórmula lactea pueda imponer a otras funciones fisiológicas. Este estudio fué planeado para evaluar cuantitativamente el aumento en la cantidad de solutos que se impone al riñón, es decir, para determinar en que extensión se reduce el margen de seguridad que tiene un niño contra la deshidratación, cuando se omiten la adición de hidrocarbonados en la fórmula láctea. Para lograrlo se comparó la carga renal impuesta por una fórmula con leche evaporada, agua e hidrocarbonados adicionales, en un grupo de 6 lactantes, con la carga renal de solutos cuando se alimentaron los mismos lactantes solamente con leche evaporada y agua, teniendo ambas fórmulas el mismo valor calórico. Una vez determinadas las dos cargas promedio de solutos renales, se calcularon los requerimientos acuosos urinarios obligados para cualquier concentración de la orina y al mismo tiempo se determinó la concentración urinaria que debe alcanzarse para cada carga renal cuando la cantidad de agua disponible disminuyó por pérdidas extrarrenales o por ingestión menor. De esta manera, la carga renal, que está relacionada con el tipo de la dieta, tiene una significación práctica real para el médico que intenta procurar un balance hídrico apropiado para el lactante.

Los resultados demuestran que la ingesta mayor de proteínas y minerales en los lactantes alimentados exclusivamente con leche y agua produjo un 85% de aumento en la carga renal de solutos comparada con la carga de la leche azucarada.

Aunque este aumento de la carga renal, y por consiguiente de los requerimientos hídricos renales, puede tener escasa significación en las condiciones normales de ingestión y gasto acuosos, reduce de todos modos el margen de seguridad contra la deshidratación. Al mismo tiempo esta carga renal mayor puede ser un factor importante que comprometa el balance hídrico y bienestar del niño, a menos que se suministre una cantidad extra de agua, cuando la ingesta se reduce apreciablemente o el gasto hídrico extrarrenal se aumenta, o bien cuando existe un obstáculo a la función de concentración del riñón.

Por consiguiente, debe enfatizarse la importancia práctica al planear el alimento del lactante considerando no solo los factores nutritivos sino también sus propiedades.

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AMERICAN ACADEMY OF PEDIATRICS, INC. PROCEEDINGS AND REPORTS

Round Table Discussion

ADOLESCENT GIRL AND HER MENSTRUAL PROBLEMS

JANET W. MCARTHUR, M.D., Boston, *Chairman*
FREDERICK B. JOY, M.D., Seattle, and ERNEST L. GLASSCOCK, M.D., Kansas City, Mo., *Secretaries*

Chairman McArthur: The first consideration of this discussion is: "Who shall take care of the menstrual problems of the adolescent girl?" Shall it be the gynecologist, the internist, or the pediatrician? My own feeling is that the pediatrician is probably the best qualified of all these specialists to handle adolescent problems. In the first place, he has usually known both the parent and the child for many years, and has gained a rapport of inestimable value in allaying the embarrassment of the patient and the anxiety of the parent. In the second place, the pediatrician has the developmental point of view. It is essential to treat adolescent menstrual disorders with patience and restraint—attitudes which come naturally to a specialist thoroughly accustomed to the vagaries of an evolving organism.

If we examine the following list, which enumerates the various sexual characteristics in the order in which they appear, we see the relevance of the developmental point of view to problems of sexual maturation. It becomes evident that adolescence is a process—not an event. Because the first menstrual period is such a dramatic occurrence one is apt to think that it is synonymous with sexual maturity, the ability to reproduce one's kind. Actually, this is not the case, as we know from several lines of evidence. Thus, anthropologists studying the inhabitants of the Trobiand Islands have found pregnancy to be rare in young girls until one to 2 years have elapsed following the first menstrual period. In these islands, it is customary for sexual congress to take place freely from childhood on. Moreover, police statistics from large cities indicate that it is quite uncommon for a girl raped within the first year or 2 after the menarche to become pregnant. It appears, therefore, that a one to 2 year period of sterility normally follows the first episode of menstrual bleeding: a period of time during which ovulation does not occur and conception is impossible.

This is a helpful outline to have in mind when one is confronted with a girl of 16 or 17 years who is brought to the physician because she has not yet had a menstrual period. If on examining the patient one can demonstrate budding of the breast, for example, one has good evidence for thinking that sexual maturation is, in fact, underway and that a menstrual period can be anticipated within the next year or 2. It is important to appreciate that the order of appearance of these characteristics

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is by no means hard and fast. The order may vary considerably without implying the presence of any abnormality, and no clinical significance should be attached to minor deviations.

From the point of view of the ovarian hormones, estrogen is the keystone of the reproductive corner. It is due to the influence of this hormone that the reproductive tract grows to mature proportions and it is in large part due to the subsequent waxings and wanings of estrogen that menstrual periodicity is established. This hormone appeared relatively early in the course of evolution, and is firmly entrenched in mammalian physiology.

Progesterone, on the other hand, appeared relatively late in evolution in response to the trend toward viviparity. In the development of the human individual, as well as in the evolution of the race, the corpus luteum is late in making its appearance (see table 1). Moreover, function of the corpus luteum is the first to drop out in the menopause and it may be resumed only slowly after a period of strain or sickness. All these observations point to the vulnerability of the corpus luteum as compared with the ovarian follicle, and it is this vulnerability which is the key to many of the disorders with which we must contend in adolescence.

TABLE 1

ORDER OF APPEARANCE OF FEMALE SEXUAL CHARACTERISTICS

Age (yr.)	Sexual Characteristics	Status of Hormone Production
3– 7	Infantile	Very small amounts of estrogens and 17-KS in urine.
8	Ovarian follicles display more advanced development. Uterus begins to grow.	Urinary excretion of estrogens and 17-KS begins to increase.
10–11	Budding of breasts. Appearance of pubic hair.	Estrogen excretion greatly accelerated.
11–12	Remolding of bony pelvis. Vaginal changes. Breasts advance to primary mamma stage. Growth of external and internal genitalia greatly accelerated.	Gonadotropins become demonstrable in urine. Estrogen excretion further augmented, becomes cyclic in character.
13–14	Appearance of axillary hair. Menarche (average age 13.5).	
14–15	Earliest normal pregnancies.	Pregnandiol appears in urine during luteal phase.
16–17	End of skeletal growth.	

Proper synchrony in ovarian hormone secretion depends, of course, on proper synchrony in the secretion of the gonadotropic hormones of the pituitary. From the physiologic evidence now available it would appear that 3 separate gonad-stimulating principles must be secreted by the pituitary in order to insure normal ovarian function. These are: (1) follicle-stimulating hormone (FSH) which promotes the growth of the follicle in its early stages; (2) luteinizing hormone (LH) which brings about ovulation and the formation of a corpus luteum and which, in combination with FSH, promotes the secretion of estrogen by the follicle; (3) luteotropic hormone (LTH) which causes the corpus luteum to secrete progesterone. In response to the stimulation of these pituitary hormones the ovary secretes its characteristic steroid hormones. During the first half of the cycle estrogen secretion by the follicle produces a rising titer of circulating estrogen; during the second half of the cycle estrogen and progesterone secretion by the corpus luteum continue until about 48 hours before the onset of the next menstrual period, when there is an abrupt decline in the blood levels of both of these hormones.

One of the hormonal tasks of the adolescent girl, therefore, is to establish a strong rhythmic interaction between the ovary and the pituitary. Until this reciprocity has developed to a point where ovulation occurs with some regularity, the endometrium undergoes sluggish phases of growth and regression corresponding to the teetering levels of estrogen secreted by successive crops of follicles. The clinical manifestation of these sluggish growth phases of the endometrium is protracted amenorrhea interspersed with irregular bleeding. Once ovulation begins to occur, the endometrium is subjected to strong rhythmic stimulation by the estrogen and progesterone elaborated by the corpus luteum, and menstruation becomes orderly. Statistical studies on the length of the menstrual cycle indicate that 30 to 40 periods must occur before mature rhythmicity is achieved; during the erratic early

cycles the adolescent is literally learning how to menstruate. One of our tasks as physicians caring for the adolescent girl is to bear patiently with the irregularities of this epoch of her life, not complicating her physiologic task by injudicious hormone therapy.

Dr. Jerome L. Kohn, New York City: Is estrogen present at all times even when progesterone is at its maximum height?

Chairman McArthur: Yes, estrogen is present throughout the cycle, but its titer fluctuates by approximately 50%.

Sex Precocity

It will be recalled that in table 1 the normal menarcheal age was given as 13.5 years. It is important to realize, however, that this figure is a statistical norm and nothing else. If one plots the menarcheal ages of a large number of girls one will obtain a normal distribution curve. The range of normal is so wide that in our clinic we feel, somewhat arbitrarily, that we need not worry very much about anyone who menstruates after the age of 8 years and prior to the age of 17 years.

In attempting to evaluate clinically the significance of a case of apparent sexual precocity or retardation a number of factors which influence the rate of sexual maturation should be taken into account: (1) Genetic. Since there is a strong positive correlation between the menarcheal ages of mothers and daughters, one worries little about the menstruating 8 year old of a mother who was an early menstruator. However, one takes a more serious view of the situation in a menstruating girl of 8 whose mother first menstruated at 17. (2) Body build. Short, stocky girls undergo more rapid sexual maturation than do tall gangly girls. (3) Climate. Stimulating climates of the sort we have in large sectors of the continental United States are associated with maximal rates of sexual maturation. Contrary to folklore, tropical climates tend to be associated with retarded rather than with accelerated rates of sexual maturation. (4) Social and economic conditions. Optimal housing and nutrition tend to promote early sexual maturation.

Confronted with a girl who meets the admittedly arbitrary criterion for the presence of sexual precocity (menstruation before the age of 8), one's first task is to decide whether the problem is one of isosexual or heterosexual precocity. If the essence of the problem is that sexual development has occurred in a qualitatively normal manner but at an abnormally early age, the precocity is clearly isosexual in type; if elements suggesting masculine development such as clitoral hypertrophy or hirsutism are present, the precocity is heterosexual in type. Inasmuch as heterosexual precocity is readily recognizable it will not be commented upon further other than to remark that it generally results from hyperplasia or tumor of the adrenal cortex.

Isosexual precocity, on the other hand, may result from a wide variety of causes. To deal with these causes in a systematic manner it is helpful to relate them to the various links in the physiologic chain whose activation leads to orderly sexual development. Hypothalamic disinhibition of the pituitary is normally followed by the release of the gonadotropic hormones which, in turn, stimulate the ovary to secrete estrogen and progesterone. The ovarian hormones then bring about the growth and development of the secondary sexual organs, the visible indication of mature sexuality. If the chain has been completely activated from the top down, the end result is ovulation and potential pregnancy. Patients in whom this process has occurred at an abnormally early age have true precocious puberty. If, on the other hand, the hypothalamic and pituitary links remain dormant but there are visible indications of sexual development due to, say, a hormone-producing tumor of the ovary or the accidental ingestion of estrogenic compounds, ovulation does not occur and the case is one of pseudo-precocious puberty.

In making this important clinical distinction between true and pseudo-precocious puberty one of the most helpful tests at our disposal is an assay of the pituitary gonadotropic hormones in the urine. If complete activation of the physiologic chain has occurred and if the gonadotropic hormones are being secreted in amounts sufficient to have brought about peripheral precocity, then the hormones will be demonstrable in the urine of the child. If, on the other hand, the chain has been short-circuited at some level below the anterior pituitary, gonadotropic hormones will not be demonstrable in the urine.

Dr. Edwin Adams Harper, Lynchburg, Va.: Is there any difference in urinary hormone excretion between cases of true precocity due to a hypothalamic difficulty from one due to a pituitary difficulty?

Chairman McArthur: While, in theory, a pituitary lesion causing sex precocity should exist, actually no such lesion has ever been recognized. Therefore, the cause of all cases of precocity having demonstrable gonadotropin in the urine is thought to be hypothalamic.

Having made the necessary clinical distinctions between iso- and heterosexual precocity and between true and pseudo-precocious puberty, let us proceed to the details of differential diagnosis. The conditions to be considered are listed in table 2.

For some reason, neurologic lesions are far less common as a cause of precocity in females than in males; only a handful of authenticated cases have been reported in females. Albright's syndrome of patchy cutaneous pigmentation, disseminated bone lesions and sexual precocity is much less rare.

Of all the causes of true precocity due to hypothalamic activation, idiopathic "constitutional" precocity is by far the commonest entity. Indeed, it is thought to account for 80 to 90% of all causes of female precocity. However, it is unsafe to assume that this condition is present. The diagnosis should be made by exclusion, and, once made, should be reviewed periodically.

Pseudo-precocious puberty develops most frequently as a result of ovarian tumors and cysts which

TABLE 2

CAUSES OF TRUE AND PSEUDO-PRECOCIOUS PUBERTY

A. True precocious puberty: Hypothalamic
   1. Destructive lesions
      a. Tumors and cysts
      b. Postmeningitic and postencephalitic lesions
   2. Idiopathic
      a. "Constitutional" precocity
      b. Polyostotic fibrous dysplasia (Albright's syndrome)
B. Pseudo-precocious puberty
   1. Ovarian
      a. Granulosa and theca cell tumors
      b. Follicle cysts
      c. Miscellaneous tumors: teratoma, chorionepithelioma, etc.
   2. Adrenal: Adrenal cortical tumors
   3. End organ
   4. Medicational: Estrogen

produce a premature supply of estrogen and hence precocious secondary sexual development. The clinical history of patients having one of these tumors depends primarily upon the fact that endocrine activity is present. Less commonly mechanical and circulatory disturbances, and occasionally malignancy, dominate the clinical picture. The syndrome presented by cases of granulosa cell tumor, the commonest of these tumors, is strikingly uniform. In most instances a whitish vaginal discharge, often periodic, is the first symptom. Later, vaginal bleeding, which may mimic normal menstruation very closely in its periodicity, occurs. The breasts hypertrophy and other secondary sexual characteristics appear. A tumor in the region of the adnexae can usually be made out by abdominal or rectal examination.

Isosexual female precocity on an adrenal basis is an excessively rare occurrence. However, precocity resulting from undue sensitivity of certain end organs to hormonal stimulation is seen not infrequently. Breast enlargement or pubic hair growth may be observed without other evidences of sexual maturation. Patients exhibiting these phenomena require careful study and prolonged observation to exclude the possibility of incipient hyperhormonal precocity.

The widespread use of oral estrogenic preparations for the relief of menopausal symptoms has increased the opportunity for accidental ingestion of these substances by children. We have recently seen 2 such cases in which the intense pigmentation of the child's nipples suggested that the estrogen was exogenous in origin.

Question: How long is required for the ingestion of estrogen before you notice clinical changes?

Chairman McArthur: That is a function of the potency and dose of the estrogen. I should think, however, that if one were making serial smears of the vaginal secretion one would find cornification in a matter of days. The other changes would, in all probability, take weeks to appear. The rate of regression, once estrogen is withdrawn, is quite rapid. Within a period of 3 to 4 weeks the vagina will revert to an absolutely atrophic state.

Dr. Thurman B. Givan, Brooklyn: Would there be any change later on in the menstrual cycle of a girl accidentally given some of these hormones?

Chairman McArthur: From studies in experimental animals it is known that protracted estrogen treatment can damage the reproductive system. The extent of the damage seems to depend upon the age at which the hormone is given, the younger the animal at the time of estrogen administration, the greater the damage. We have debated this question in our own clinic in connection with girls who were growing excessively tall and whose epiphyses we wanted to close with estrogen. Although little clinical experience is available for guidance, it seems probable that if estrogen is not given too early in puberty it can be administered with reasonable safety.

Bleeding

Definition of what constitutes abnormal bleeding, like the definition of what constitutes sexual precocity, must of necessity be somewhat arbitrary. In our clinic we feel that bleeding which lasts more than 7 days, which is sufficiently profuse to produce symptoms of blood loss such as palpitation, weakness and dizziness, or which is severe enough to lower the hemoglobin should be regarded as pathologic and should be carefully investigated.

There are many ways in which the causes of bleeding can be classified. One which we have found convenient in this age group is shown in table 3:

TABLE 3

CAUSES OF MENORRHAGIA IN ADOLESCENCE

1. Endocrinopathies
   a. Metropathia hemorrhagica ("functional uterine bleeding")
   b. Estrogen-producing tumors
   c. Stein-Leventhal syndrome
2. Constitutional diseases
   a. Blood diseases
   b. Liver disease
3. Local pelvic pathology
   a. Complications of pregnancy
   b. Tumors of vagina and cervix

Of the entities listed metropathia hemorrhagica accounts for more cases of menorrhagia than all the others put together. However, it is unsafe to assume that one is dealing with this disorder without having made a diagnostic survey designed to exclude other causes of bleeding. The history and general physical examination occasionally provide clues which lead to the immediate recognition of constitutional diseases underlying the menorrhagia, such as scurvy or leukemia. More frequently, however, the general examination must be supplemented by additional studies if the diagnosis is to be firmly established.

Of these additional studies, one of the most important is examination of the pelvic organs. Because the adolescent girl may become tense and frightened if any attempt is made to examine the genitalia, one can gain a good deal more information about the pelvic viscera by making the examination under anesthesia. If the patient is bleeding so profusely that a curettage is necessary in order to check the hemorrhage, one has an ideal opportunity to inspect the cervix and to palpate the uterus and adnexae. A curettage is, of course, the most rapid and effective way of stopping bleeding; it can be depended upon to secure temporary hemostasis even if the underlying difficulty is thrombocytopenia. If one does a curettage, it is worth while to have the curettings examined histologically. As will be pointed out later, the character of the endometrial histology is of the greatest assistance in planning the program of therapy.

If the bleeding is not sufficiently alarming to necessitate curettage under anesthesia, the state of the pelvic viscera can still be evaluated with fair accuracy by recto-abdominal examination in the conscious patient. With practice, the pediatrician can gain an idea of the size, position and consistency of the uterus and the adnexae. Except in the small percentage of girls in whom the hymeneal ring is excessively tight, a little care, patience and gentleness will enable one to visualize the cervix with the help of a small duckbill speculum. Under these circumstances a vaginal smear should be substituted for the endometrial biopsy so that some idea of the estrogen level may be secured.

To exclude blood dyscrasias one should first of all examine a carefully-prepared blood smear; the smear may provide the first clue to the diagnosis of thrombocytopenic purpura or leukemia. The

bleeding time and the tourniquet test take little time to do and may help to clinch a diagnosis of thrombocytopenic purpura, or to suggest the presence of pseudohemophilia. For determination of the bleeding time we use a modification of the Ivy method. An incision 3 mm. long and 3 mm. deep is made in the volar surface of the forearm with a number 11 Bard-Parker scalpel blade, 40 mm. of pressure being maintained on the arm throughout the procedure by means of a blood pressure cuff. A fresh blade is employed for each patient. The incision is then blotted every 30 seconds with a piece of filter paper, care being used not to touch the edges of the wound. A normal person ordinarily stops bleeding within 6 minutes. The clotting and prothrombin times have seldom proved helpful, although occasionally they provide decisive information, as in the case of a student nurse whose bleeding we could not explain until we found her blood to be incoagulable and her prothrombin time tremendously prolonged. This mystified us because she seemed to have no liver disease or other cause for prothrombin deficiency. We finally learned that she had erroneously thought herself to be pregnant and had attempted to induce an abortion by ingesting dicoumarol.

Let us now proceed to the pathologic physiology and treatment of functional uterine bleeding. Clinically, this syndrome is characterized by long periods of amenorrhea interspersed with periods of painless bleeding which may continue for days, months, or even years. Fatal bleeding is rare but chronic debility from blood loss anemia is not infrequent. If one inspects the ovaries of one of these patients one finds that they contain numerous follicles, and often a large follicular cyst, but no corpora lutea. The endometrium corresponds pathologically to the ovarian findings; that is, the endometrium lacks secretory differentiation. The implication of these endometrial findings is that too little estrogen has acted for too long a time in the absence of progesterone. Most of us were taught that the metropathic endometrium is characteristically proliferative in type and that the "Swiss-cheese" endometrium is the classical expression of hyperplasia. More extensive studies have confirmed the correctness of the interpretation but have shown that in adolescent girls the degree of hypoestrinism is frequently more severe than was originally thought. The rate of estrogen secretion is often too low to lead to "Swiss-cheese" hyperplasia; it may be so low that it induces no endometrial growth whatever. Upon curetting the uterine cavity of such an individual one obtains either a wisp of atrophic endometrium or no endometrial tissue whatever. (Or, if one has substituted a vaginal smear for the endometrial biopsy, one finds the smear devoid of cornified cells; basal cells, precornified cells and leukocytes are the only cellular elements which are recognizable.)

From what was said initially about the role of estrogen as a growth hormone for the female reproductive tract, the reason for the occasional findings of an atrophic endometrium is apparent. In individuals with metropathia hemorrhagica a mature reciprocal relationship between the pituitary and the ovary has yet to be established. Crops of follicles start to mature, but do so sluggishly and fail to undergo the spurt of midcycle growth which culminates in ovulation and corpus luteum formation. Instead, they undergo atresia only to be succeeded by a new crop of follicles. The level of circulating estrogen is abnormally low, and instead of undergoing strong rhythmic variations it teeters up and down. When the level of estrogen declines, the endometrium regresses and undergoes surface necrosis but full-scale desquamation does not occur.

Upon beginning the treatment of these patients it is important to reassure them strongly concerning the eventual outcome of their difficulty. Although it is seldom that these patients express their anxiety, many fear that the bleeding implies gross abnormality of their reproductive organs and ultimate sterility. Such meager statistics as are available indicate that reproduction is not impaired in women who have had metropathia. Therefore, having made a careful examination of the pelvic organs, the physician is in a position to give convincing reassurance. At the same time that one informs the patient that time is on her side, it is important to acquaint her with the fact that relapses are frequent and that many courses of hormone therapy may be required before she begins to menstruate with any degree of regularity.

The nature of the hormonal therapy employed depends upon the degree of hypoestrinism present. If the histology of the endometrium or the cytology of the vaginal epithelium indicates that the level of circulating estrogen is not excessively low, treatment with courses of progesterone alone may suffice. If one gives intramuscular injections of progesterone in oil in a dose of, say 5 mg. a day for 5 days, withdrawal bleeding will follow within approximately 48 hours after the last injection of progesterone. This amount of progesterone does not, of course, suffice for the formation of a secretory endometrium. If progesterone were not so expensive it would undoubtedly be better to give a larger dose for a longer time, thereby simulating the function of a normal corpus luteum. How-

ever, if the level of endogenous estrogen is adequate to "prime" the endometrium (progesterone is almost inert, biologically, in the absence of such priming) a satisfactory withdrawal flow will result. If such courses of progesterine be given approximately every 6 weeks (intervals of 4 weeks may not allow enough time for the deficient ovarian secretion to prime the endometrium) metropathic episodes can be prevented.

How can one tell when to stop the therapy? Our criterion is the occurrence of the "escape phenomenon," as Albright calls it. By this is meant failure of withdrawal bleeding to occur within 48 hours of the last injection of progesterone. If several days elapse before the beginning of bleeding one can conclude that ovulation must have occurred and that a corpus luteum has been supplying progesterone in amounts far larger than those injected. The patient therefore continued amenorrheic until the corpus luteum completed its span of life, and when it waned bleeding began. To be sure, one's therapeutic troubles are not necessarily over when an "escape phenomenon" occurs—as has been previously stated considerable retreatment may be required. Nevertheless, the occurrence of an escape is a mark of progress and warrants temporary discontinuance of therapy.

If hypoestrinism is severe, therapy with progesterone alone is destined to fail. One must first use estrogens, sometimes in surprisingly large doses, to induce endometrial growth and to prime the endometrium for the action of progesterone. A daily dose of as much as 6 mg. of diethylstilbestrol may be necessary initially in order to check bleeding. In subsequent cycles it is our practice to reduce the dose of estrogen as rapidly as possible. After two or three 21 day courses of estrogen we add progesterone to the program, giving 5 mg. in oil daily during the last 5 days of the course of estrogen and stopping the 2 simultaneously. Eventually, estrogen can be omitted altogether and progesterone alone used as previously described.

What must be prevented at all costs is the performance of hysterectomy in these adolescents. This is a tragedy for which there is no longer any excuse. If patients have been rendered severely anemic by acute hemorrhage they can be sustained by transfusions and their bleeding checked by curettage. The menstrual and reproductive function of these individuals can be salvaged, if only sufficient patience and restraint is exercised in therapy.

Amenorrhea

Amenorrhea should be regarded not as a disease but as a symptom. In dealing with adolescent patients, it is helpful to distinguish between those individuals who have never menstruated (delayed menarche) and those in whom there is a cessation of menses previously present (postmenarcheal amenorrhea). Patients with delayed menarche, in turn, can be subdivided into 2 categories: (1) patients in whom amenorrhea is the reflection of a complete absence of sexual development and (2) patients in whom sexual development appears to be normal in all respects except for the occurrence of menstruation.

A point of some practical importance should be mentioned at the outset, and that is that the laboratory studies required for adequate study of an obscure case of amenorrhea are very expensive. From the diagnostic point of view, the work-up of a patient with amenorrhea must generally be far more extensive than that of a patient with bleeding. It is important, therefore, to make a purely clinical diagnosis if this is at all possible.

The first essential is an accurate history with emphasis on: (1) the family history as regards endocrine disorders, such as unusually early or late puberty, and familial hirsutism, (2) the character and duration of any illness preceding the amenorrhea, (3) a precise description of the patient's menstrual history—a calendar should be constructed by the physician showing the dates of all periods whose onset can be accurately recalled, the duration of flow, and any midcycle or menstrual symptoms and (4) the habits of the patients as regards rest, diet and recreation. An attempt should be made to assess the maturity of the patient's emotional adjustment.

A complete physical examination is carried out and particular attention paid to the presence of systemic disease, the type of body build and the presence of the secondary sex characteristics. The optic fundi are examined and the visual fields outlined by confrontation. The external genitalia are inspected and the uterine dimensions estimated by means of recto-abdominal examination. Vaginal examination can usually be omitted unless the preliminary findings suggest the presence of developmental anomalies of the genitalia.

If systematically carried out, even this limited scrutiny will enable certain conditions associated with amenorrhea to be recognized at a glance or diagnosed after a minimum of investigation:

adrenal insufficiency and hyperfunctioning lesions, hyper- or hypothyroidism, diabetes mellitus, chronic infectious and debilitating diseases, nutritional disturbances (such as obesity and undernutrition), developmental anomalies of the genitalia and pregnancy.

If the cause of the amenorrhea remains obscure after the preliminary evaluation, it must be sought by means of procedures which test separately each link in the uterine-ovarian-pituitary-hypothalamic chain upon whose integrity normal menstrual function depends. In actual practice, the most important point to determine initially is whether the amenorrhea is ascribable to pituitary or ovarian failure. This can be ascertained by assaying the urine quantitatively for the presence of gonadotropic hormones. If the pituitary is at fault, gonadotropins are absent from the urine; if the ovary has failed, gonadotropins are present, generally in amounts greatly in excess of normal.

Question: Why is there a high level of gonadotropins at the menopause?

Chairman McArthur: Because of the fact that failure of the ovary results in withdrawal of the normally inhibiting effect of estrogen upon gonadotropin secretion. The ovary runs out of ova and, in consequence, there are no more follicles to develop and make estrogen. In rare instances, the ovary fails completely in adolescence, and the girl is precipitated into the menopause.

The occurrence of amenorrhea despite normal amounts of gonadotropins in the urine suggests that the hypothalamus may be at fault. It is important to be alert to this possibility, because adolescents are unusually prone to have "hypothalamic" amenorrhea. Such apparently trivial disturbances as going away to school for the first time or entering nurses' training may produce amenorrhea in susceptible individuals. Girls who do not have underlying emotional instability of a serious sort generally recover spontaneously as they become adapted to the new environment. However, the time required for their recovery may be greatly shortened by judicious reassurance.

Rational therapy of the amenorrheas is clearly dependent upon precision in diagnosis. In amenorrhea due to serious congenital anomalies of the uterus or vagina, it is manifestly impossible to induce menstruation by means of cyclic hormone therapy. If such a patient shows normal feminine secondary sexual development, there is nothing to be gained by hormonal treatment. Hypothalamic amenorrhea due to transient stress is ordinarily self-limited although psychotherapy may be required for prolonged amenorrhea resulting from serious emotional disturbances. Patients with a precocious menopause should be given the benefit of cyclic replacement therapy with estrogen.

Dysmenorrhea

Discomfort of one kind or another at the time of the menses is experienced by the majority of women at some time or other during their reproductive lives. They may complain of lassitude, irritability, depression, urinary frequency, headache, gastrointestinal symptoms such as constipation or diarrhea, and bearing-down sensations in the pelvis. In some women, the pelvic discomfort attains the proportions of pain and may prove incapacitating. Such pain is termed dysmenorrhea.

When dysmenorrhea occurs in the absence of demonstrable pelvic pathology it is defined as "primary"; when associated with organic gynecologic lesions, as "secondary." The various pelvic disorders of which dysmenorrhea is sometimes a symptom (endometriosis, pelvic inflammatory disease, etc.) are extremely rare in adolescence. However, examination of the pelvic organs should not be omitted on this account; it will confirm the diagnosis and reassure the patient.

Little is known concerning the cause of primary dysmenorrhea. However, it appears that cramps are in some way related to the occurrence of ovulation. Bleeding from a proliferative endometrium, unless it is so rapid as to involve the expulsion of clots, is almost invariably painless. The clinical evolution of dysmenorrhea in adolescence also lends support of the concept that ovulation is a *sine qua non* of primary dysmenorrhea. After a year or so of painless periods, the adolescent often begins suddenly to experience cramps. Presumably, the first periods are anovulatory and dysmenorrhea signifies the beginning of mature ovarian function and corpus luteum formation. Dysmenorrhea reaches a peak of intensity around ages 18 to 20 with a gradual decrease in intensity thereafter. but many women retain their complaint at its original intensity long after this age is well passed.

That psychologic factors are important in dysmenorrhea is suggested by the absence of organic pathology and by a number of other considerations: (1) The menses are conspicuously susceptible to delay or to anticipation, as is well known from the occurrence of "hypothalamic" amenorrhea and from the high incidence of menstruating brides. (2) Dysmenorrhea is amenable to divers treatments. (3) The chief symptom of dysmenorrhea is pain, in whose evaluation there is inevitably a strong subjective element.

In a study of dysmenorrheic adults, Wittkower and Wilson found that these patients were of 2 chief types. There was a well-defined group whose members tended to be physically immature. As children many of them were timid, overly attached to their parents, and deeply self-conscious. They were partially resigned to their menstrual periods but still objected to them on the grounds of being offensive to their sense of fitness and cleanliness. The menarche was disturbing as signifying the end of their childhood. They craved affection and sympathy, tended to overestimate their illnesses as children, and to follow this through with an overreaction to their menstrual periods, treating them as an illness and using them to get the affection they craved.

The second group of Wittkower and Wilson was a boisterous one—an aggregation of tomboys who felt deep resentment toward their feminine role. As children these women had been overly attached to their fathers, contradictory in relation to their mothers, and openly jealous of their brothers. They were resentful of menstruation from its onset because of its "messiness." They regarded their periods as a handicap in competition with males and were anxious only to be "sisters" to men. Those among the group who were physically attractive used their charm as a means of humiliating men.

The therapy of dysmenorrhea is to a certain extent prophylactic. By teaching girls that menstruation is a normal physiologic function during which no essential modification of their ordinary activities is necessary, much can be done to help children of the first type, those prone to develop a hypochondriac attitude toward menstruation. On the other hand, simple prophylactic therapy is patently inadequate to help girls of the second type, those in whom menstrual pain is a symptom of dissatisfaction with and hostility toward their feminine role. Let us consider in greater detail the problems of the tomboy group.

It should be realized, first of all, that menstruation is uniquely a mark of femininity. Not all women bear children but all women except for a few abnormal ones do have, for a period in their lives, a cyclic issue of blood. During the period between childhood and senility menstruation is a constant reminder of femininity, welcome or otherwise. Moreover, menstruation is a symbol of differentiation between the roles of female and male, for to be a female is also not to be a male. Whatever may have been her wishes prior to menstruation, with the menarche the pubescent girl becomes committed to femininity and experiences either happy anticipation of female duties, responsibilities and privileges or bitter resentment of all these. In signifying mature femininity, menstruation is threatening in that it implies independence from the mother and competition with her. Past relationships with the mother are infused with a new meaning that may be marked with tenderness or hostility. If there is a good relationship between the premenarcheal girl and an accepting, loving and secure mother, the girl may identify with her and thus accept femininity. If, on the other hand, the mother exemplifies an over-anxious, ashamed or hostile reaction toward menstruation or sex, difficulties may arise for the girl.

The complexities inherent in the treatment of the tomboy dysmenorrheic are apparent. If time does not reconcile these unhappy adolescents to their feminine role and if dysmenorrhea continues, the advisability of psychotherapy should be seriously considered. These patients often relate in a surprisingly compliant fashion to kindly, accepting authority figures such as a physician and may be greatly helped by comparatively brief psychotherapy.

In less serious cases, adequate relief of pain can often be provided by means of periodic self-medication with mild analgesics. In more refractory cases, an occasional respite from dysmenorrhea can be given by therapy designed to inhibit ovulation. If estrogen, say diethylstilbestrol in a dose of 1 mg., is given daily for 21 days starting on the first day of menstruation, ovulation is prevented and the subsequent period is painless. Such a course of estrogen treatment should be given early in the management of patients who have had severe pain not benefitted by ordinary analgesics. The occurrence of a pain-free period may hasten recognition of the fact that dysmenorrhea does not necessarily imply an abnormality of structure nor need it be the inevitable accompaniment of menstruation. Indefinite continuation of such courses of estrogen is, unfortunately, not practicable since after 2 or 3 cycles metropathic bleeding will ensue. However, estrogen can be held out to the patient as a prophylactic agent which can be depended upon when cramps threaten the enjoyment of some special event, such as high school graduation or the senior "prom."

Round Table Discussion

PSYCHOLOGICAL DISTURBANCES DURING ADOLESCENCE

WILLIAM S. LANGFORD, M.D., New York City, *Chairman;*
REYNOLD A. JENSEN, Minneapolis
MILTON M. GRENNBERG, M.D., Washington, D.C., and HAROLD D. LYNCH, M.D.,
Evansville, Ind., *Secretaries*

Chairman Langford: In the personality and physical growth of the individual there are some periods when the task of adjustment is a little more difficult than others. We see it at weaning, when the child starts school, at adolescence, on his first job, later when he gets married and—one of the most severe trials of all—when the individual becomes a parent. About 90% could be called normal disturbances in this area of adolescence and psychologic disturbances.

Dr. Cornelia M. Carithers, Jacksonville, Fla.: When you see a marked problem such as rivalry between children, how do you convince the parent it is a real problem?

Chairman Langford: One of the more common instances is the jealousy of the younger child for the older child. This may enter the picture with the obese child. Often it is the younger child who will become obese for the satisfaction he gets out of the tremendous body size. The problem of obesity may be of particular significance in the adolescent period. It may be a phase that many children go through as part of this gradual growth process but it also may be related to other factors; this suggests that when dealing with a child who is heavier than he or she should be, one ought to individualize each child who presents the problem. Therefore, it is necessary for those of us who deal with these children to determine what is a normal gain in weight for a period of time and what is outside the range of normal. It may involve the adolescent in that he or she is also worried about the obesity. It may be a problem which is primarily for the family to solve. The problem that you and I have may be because we feel a sense of frustration and of not knowing just what to do or how to approach the problem. As we approach the problem, again individualizing it, it is necessary for us to determine as we go along what the main sources of the difficulty are. If we know it is chiefly concerned with the child, then we can direct our energies more toward the youngster.

As far as some of the psychologic aspects of this problem are concerned it may go way back to earlier experience; this suggests that perhaps if we anticipate the problems that are coming up with the families whom we serve, we can help shape and direct the attitudes of a parent toward a youngster who may be obese. It is often evident that this previous experience of the child is accentuated now in the very stressful period-adolescence.

Dr. Hyman C. Tolmas, New Orleans: In my practice I have encountered an overzealous father who cannot see his son doing anything he didn't do when he was a boy. He feels that the child should toe the mark, so to speak.

Chairman Langford: Many times it may be that you will serve in a substitute role of the parent in guiding the anxious adolescent. One must consider family patterns, including dietary patterns, family situations, tensions. If the adolescent has had a reasonably satisfactory experience in the infancy period and early childhood, even though he presents problems in adolescence, he is prepared to ride through the stressful period much more easily and successfully than if his early adjustment and experience was unhappy.

Question: What are the basic factors contributing to obesity in the adolescent?

Chairman Langford: It may be a deep seated psychologic problem and those are extremely difficult to deal with but then again it may be a reaction to some reality problem or then it is symptomatic of some other disorder.

Dr. John T. Barrett, Providence, R.I.: Many mothers have developed guilt complexes because they feel they are not doing the right things towards the development of their children according

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Presented at the Annual Meeting of the American Academy of Pediatrics, Chicago, Oct. 20 and 21, 1952.

to the articles presented to them in the current women's magazines on problem parents, etc. How can you handle those mothers?

Chairman Langford: As pediatricians it may be helpful for us to interest ourselves in the education of the parent in the clarification of their problems and in giving them support in their decision. Often by just letting the parent talk, the situation will right itself.

Robert J. McKay, Jr., Burlington, Vt.: The chief problems of mothers who have consulted me about their adolescent children have been in regard to morals in the schools.

Chairman Langford: The problem here is due not necessarily to their home upbringing, but to their conflicts between their desire to join the group and the moral principles with which they have been brought up.

Some of these problems arise at this period with the "keeping up with the crowd" attitude when economic conditions in the home are lower than those of the associates of the adolescent. Then, on the other hand, we have the adolescent trying to separate from parental influence, yet not knowing how to do it. This area in the adolescent has to do with emancipation and achieving self-independence. In joining up with groups the youngster has 2 masters—serving the group and his parents. Problems also arise in the uneven development of sexual maturity.

Dr. J. Victor Greenebaum, Cincinnati: My problems arise when the mother says her child resists everything. I advised one woman to read the book *The Age of Resentment* aloud with her daughter for a closer understanding between the two. I also give them other books that I have received from the government for I have found that reading helps them understand this period.

Dr. Jensen: At this period we have the youngster in a state of constant criticism of his parents and if we can help parents to realize that this will pass and it develops that the child will achieve definition within himself—it is his struggle for independence. This process of growing is an up and down affair. It isn't a straight smooth line and it is common for a girl to act like a lady one day and the next day be out playing cowboys and Indians. Parents themselves vacillate between wanting their children to grow up and wanting them to remain children.

Dr. Gladys C. Winter, Teaneck, N.J.: We can greatly sympathize with parents who do not have the knowledge of what they should expect from the adolescent.

Chairman Langford: I would like to stress the fact that in this struggle for self-dependence, after all, we expect the child, when he gets through these developmental periods, to be a reasonably self-sufficient adult who can arrive at decisions on his own pretty well. The process is going on from the state of extreme dependency in the newborn child to this self-sufficient adult. Biologic maturity comes along some place in adolescence. As far as the things we permit the child to do, he remains encased in a certain amount of dependence, financially, legally and many other ways until he is long past the period when he could be independent. He is not like the Indian child of days gone by who lived in the woods by himself for a few days, then came back to be accepted as an adult in the tribe. During the adolescent period there is a strong drive at the youngster—the parents want the child to be more mature, society wants the child to be more mature, etc. In our desire to be good to children we are delaying the achievement of independence through economic and emotional dependency upon the parent. Therefore, the child is rebellious or does not want to get out from under parental supervision.

Dr. Nelson William Ryan, Cincinnati: The significant and psychologic problems of adolescence occur in youngsters whose parents have and probably still have emotional and psychologic problems.

Dr. Jensen: Assuming that is true, and I presume it probably is in most cases, as a psychiatrist, would you suggest that work be concentrated entirely on the adolescent or with both parent and child?

Dr. Ryan: You can do very well working with the child psychiatrically.

Dr. Otto Grob, Detroit: We have discussed some of the things which bother us with the adolescent patient, but how can some of the problems of adolescence be avoided or prevented before this stage of growth?

Dr. Jensen: No general statement or line of action can really be applicable to the period because it is something that you have to take up on an individual basis. I have known a good many adolescent children who have had complaints but as time went on they became very mature and good citizens. On the other hand, a small group of them were quiet and withdrawn, did not participate in any activity, and proved to have some underlying disorder that portended later difficulty.

New Speaker: Don't you think that we could eliminate a lot of the problems of adolescence that

come down to resentment of parents if in the early years parents would get into the habit of giving the reason for their request? A command to do something builds resentment if an explanation is not given.

Chairman Langford: You are suggesting that the struggles that are accentuated in adolescence stem from difficulties that have been going on years and years before.

First Speaker: No, I thought that would be one way of easing them into the period.

Dr. Jensen: Adolescence is a particular period of life when stress and strain is increased due to the independent feeling that must be resolved if the individual is to become an independent being. Yet the nature of the struggle is dependent upon what happened before. In the course of our everyday work with the children and families we should begin helping to resolve these problems even in the period of infancy. It seems to me that from the ages of 1 through 3 most of our effort be directed toward the parent—clarification of parental questions, helping the parents to define their role in this area and giving them strength to carry through our suggestions by sharing their troubles with them. From that point on we should deal with the youngsters.

It is possible to deal less with the parent and more with the child until you come over into the adolescent years when you devote your major attention to the adolescent who is caught in whatever the struggle is, not neglecting the parent. As physicians we do a service to the parents, whose youngsters we are working with, to keep them informed—not only in what we talk to the adolescent about, but the severity of the problem and the nature of the struggle and whether we feel he is making any progress with us. We must define our role in helping the adolescent by giving thought to basic principles which will help to resolve the problems of the child. We physicians should give increasing attention to the family organization, family attitude, etc. We also might take a more active role in supporting community projects that may be important to the proper development of the adolescent.

Chairman Langford: We all know that we have a prophylactic job to be done. Nobody now pretends that their practice includes only the promotion of physical development because part of a comprehensive pediatric practice includes mental health and personality growth and development. A very large part of the pediatrician's time is taken up with this.

As physicians, our primary sources of concern has always been with the diseases and disorders and we immediately begin to think in terms of pathology and if you look through what has been written, it is difficult to try to find a definition of normal, healthy, constructive parent-child relations.

Symposium

HYDRAZINE DERIVATIVES OF ISONICOTINIC ACID

BRET RATNER, M.D., New York City, *Chairman;* EMANUEL GRUNBERG, PH.D., Nutley, N.J.; J. C. BURKE, New Brunswick, N.J.

EXPERIMENTAL CHEMOTHERAPY AND RESISTANCE

EMANUEL GRUNBERG, PH.D.

The discovery of streptomycin has shown the way by which therapeutic activity against the causative agent of tuberculosis can be found and evaluated in the laboratory prior to its administration in patients. A great number of substances synthesized by the chemist in his laboratory or isolated from natural sources have been found to exert activity against the bacillus of tuberculosis. Many of these show this effect only in the test tube and prove without effectiveness if studied in experimental animals infected with tuberculosis.

The new antituberculous agent, isonicotinic acid hydrazide (rimifon®), is a rather simple synthetic compound which was found to be superior to known antituberculous drugs during early stages of the laboratory investigation. Rimifon® possesses not only a remarkably high growth inhibiting effect against the tubercle bacillus in the test tube but also unusual features if studied in infected animals. Most of the fundamental work which has been confirmed in laboratories all over the world was done in mice which were infected with high and fatal doses of human tubercle bacilli. In this infection rimifon® showed 4 characteristic properties which had not been observed with any of the known drugs: (1) the drug protected heavily infected mice after administration of very small doses, (2) the drug successfully prevented the multiplication of the tubercle bacilli in the infected tissues of the animal and therefore (3) produced a lasting protection after discontinuance of therapy, and (4) if given therapeutically in animals in which the disease had already produced its characteristic lesions the drug tended to stop further development of the disease and to prepare the ground for the final cure.

In sharp contrast to the broad spectrum antibiotics acting on a multitude of pathogenic bacteria and even viruses, rimifon® is a specific drug in the strict sense of Ehrlich's concept of chemotherapy in that it exerts its activity only against the group of mycobacteria of which the most important representatives are the tubercle bacillus and bacillus of Hansen's disease (bacillus leprae).

Like all drugs of high potency rimifon® also produces drug-resistant strains. This phenomenon can be demonstrated in the test tube but has so far not been observed in infected animals although it has been seen in about 5 to 10% of the cases of human tuberculosis treated with this agent. It is well known that also the administration of our leading drug against tuberculosis, streptomycin, quite frequently leads to highly resistant strains of tubercle bacilli. One has learned that combination therapy overcomes this unfavorable feature of streptomycin to a certain extent and studies are presently under way to determine whether drug resistance to rimifon® can be delayed or overcome by combination of it with other antituberculous substances.

THE PHARMACOLOGY OF ISONIAZID

JOHN C. BURKE, PH.D., and BERNARD RUBIN, PH.D.

Isoniazid has been shown to be an effective antituberculous agent both in experimental and human tuberculosis. The purpose of this paper is to describe some of the pharmacologic properties of this class of drugs.

Absorption, Distribution and Elimination: Isoniazid is readily absorbed from the gastrointestinal tract. Peak blood levels are usually achieved within ½ to 2 hours in the dog or man, and is closely predictable from the dose. It is distributed in most tissues and its concentration in these tissues follows the plasma concentration quite closely.

The rate of disappearance of the drug from the plasma is about 19% per hour in the dog and

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about 17% per hour in man. Approximately 25 to 50% of the isoniazid administered to dogs is eliminated in the urine apparently unchanged. Another 30 to 50% is converted to isonicotinic acid before elimination. This situation is closely paralleled in man.

Toxicity: The acute lethal dosage of isoniazid in most species tested is very similar for either parenteral or oral administration. Death occurs after convulsions, generally in ½ to 2 hours after dosage. The lethal plasma concentration of isoniazid in mice is at least 87γ cc., while the acute lethal intravenous dose in the dog is about 50 mg./kg. body weight.

Degree and severity of chronic toxic signs in dogs with isoniazid were proportional to dosage and survival time inversely proportional to dosage. Slight or transient anemia appeared with not more than 10 to 15% reduction in hemoglobin and RBC. Severe toxicity has been found only at more than 3.5 times current clinical dosage and was characterized by progressive occurrence of anorexia, central nervous stimulation, and fatty degeneration of the liver which may be accompanied by jaundice. Occasionally some pathology of the kidneys has been observed.

Pharmacodynamic Action: At the equivalent of current clinical dosage or plasma concentrations isoniazid apparently manifests no acute pharmacodynamic action on respiration, basal metabolism, ECG, heart rate, systemic blood pressure and peripheral resistance, neuromuscular transmission or urine output in experimental animals. Postural hypotension has not been observed. Little or no effect has been noted on autonomic ganglia, specifically cervical sympathetic, adrenomedullary or vagal. Neither has the compound shown antipyretic nor analgetic effects in animals. There has been no evidence of antihistaminic or epinephrine-like action on bronchiolar or intestinal smooth muscle.

No atropine-like effect has been observed on the pupil, on salivary secretions, nor on the heart, intestine or bladder, although one report of antagonism to cholinergic bronchospasm in the guinea pig has appeared.

In summary it may be pointed out that isoniazid is pharmacologically well suited for chronic chemotherapy. The drug may be used orally, it is both well absorbed and distributed in the body including the spinal fluid. Localization or cumulation does not appear to occur. High kidney concentrations are apparently related to the mode of excretion. Drug toxicity in man has appeared to be negligible or minor in nature. Toxicologic characteristics of isoniazid, however, indicate the continuing need for cautious dosage in hepatic or renal insufficiency, and appropriate sedation in patients with known or suspected convulsive tendencies.

CLINICAL EXPERIENCE WITH ISONIAZID IN CHILDHOOD TUBERCULOUS MENINGITIS*

BRET RATNER, M.D.

The new isoniazid group of drugs has aroused considerable interest and hope for the eventual conquest of tuberculosis. The results first achieved by Robitzek, Selikoff and Ornstein have been substantiated by others.

The isoniazid derivatives, like other chemotherapeutic agents, should be used as adjuncts to well tried measures such as surgical procedures, collapse therapy and bed rest.

In certain situations streptomycin and para-aminosalicylic acid should be employed in conjunction with these newer drugs. Drug resistance may be reduced or prevented when they are administered conjointly.

The isoniazids are signally free of toxicity and oral administration makes them invaluable, particularly for sections of the world where injectant materials would be difficult to use.

On the Pediatric Service of Sea View Hospital and New York Medical College an evaluation is being made of their effectiveness in tuberculous meningitis, primary and cavitary pulmonary tuberculosis. Isonicotinic acid hydrazide (rimifon®) and to a lesser extent the isopropyl derivative of isoniazid (marsilid®) are the drugs used.

We have for evaluation 8 cases of tuberculous meningitis treated with streptomycin and/or isoniazid.

In the first case (RW) a child with miliary tuberculosis treated with streptomycin, P.A.S. and promizole was cured of pulmonary tuberculosis but developed, while on this therapy, meningitis that

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* This study was done in the Pediatric Division of Sea View Hospital and New York Medical College, in collaboration with Drs. George Romuald Klimkiewicz, Joseph Dolgin, H. John Malone, Mary Retsina and Eduardo Margado.

deteriorated progressively. At this time when the glucose was 17 mg./100 cc. and the cell count 173 he was put on rimifon® alone and made an uneventful recovery. Within 3 months he became a healthy child. Five months of further treatment showed no exacerbation and finally, in the last 4 months, with no treatment, he has remained well mentally and physically, with normal spinal fluid components.

The second case (DC) was a child who apparently recovered from meningitis with streptomycin and P.A.S. therapy of 2 months' duration. This child was then placed on rimifon® alone and has had no exacerbation of her meningitis for a period of 5 months. Her spinal fluid findings have been normal for the past 5 months.

The third case (LF), one of miliary tuberculosis treated with streptomycin and P.A.S., cleared of pulmonary tuberculosis but developed meningitis. Rimifon® was then given alone. After 35 days her spinal fluid still contained M. tuberculosis but after 51 days more became sterile. Despite the fact that her spinal fluid became sterile, with normal values of the various components, she died from hydrocephalus 6½ months after rimifon® was started. One is tempted to assume that though she showed a residual tuberculous involvement of her leptomeninges at necropsy, her tuberculous process was on the road to recovery for the brain, lungs and all other organs were free of tuberculous pathology.

The fourth case (BR) was an infant with primary tuberculosis, treated at the inception of her meningitis with rimifon® alone, and made a complete recovery in 2 months. She was observed for 5 more months and remained clinically free of meningitis with spinal fluid normal in every respect.

The fifth child (NP) with miliary tuberculosis, meningitis and cerebral localization was treated with streptomycin, then received rimifon® alone. She died of meningitis 4½ months later.

The sixth case (GH), treated with streptomycin and P.A.S., developed decerebrate rigidity. The child was a mental vegetable. After about 6 months of this therapy, rimifon® was started. He still remains a decerebrate individual after 9 months of isoniazid therapy but his spinal fluid components are normal.

The seventh case (WF) was a child treated with rimifon® alone for one month. Because of slow improvement he has been on rimifon® with streptomycin and P.A.S. for the past 3 months. The spinal fluid components have been normal for the 3 months but the child still has spastic and cerebral involvement. Further observations are in progress.

The eighth case (DW) after 2 months of rimifon® and a combination of streptomycin, P.A.S. and marsilid® still shows abnormal spinal fluid findings. Further observations are in progress.

Rimifon levels were determined in the blood plasma and spinal fluid in a number of cases. There is evidence that this antituberculosis drug does penetrate into the cerebrospinal fluid.

This group of drugs augurs the possibility of being ancillary to streptomycin when streptomycin has failed to achieve its result. Second, it may be very valuable in cases which appear to be arrested tuberculosis treated with streptomycin, but in which instances exacerbations have been known to occur. The use of isoniazid may prevent such exacerbations. Lastly it may become a drug of great value in the prevention of tuberculous meningitis when given during the course of cavitary, progressive primary or miliary tuberculosis.

One cannot deny that streptomycin has earned an important and enviable place in the therapy of tuberculosis. However, its toxic effects, particularly that of deafness which may become permanent, the necessity for giving this drug intramuscularly and intrathecally and the tendency for M. tuberculosis to become resistant to it, prohibit its widespread use throughout the world.

It would be foolhardy at this time for us to state that exacerbations will not occur in our cases detailed above and a much larger period of observation will have to be made before such a hopeful conjecture can be substantiated.

The essential thing for us to do is to attempt a wide investigation of this drug to prove whether certain strains of M. tuberculosis will become resistant to it and to determine whether the giving of streptomycin combined with isoniazid may actually hinder the progress of sterilization of the spinal fluid.

We feel that there is enough evidence to justify the use of isoniazid alone in the treatment of tuberculous meningitis. If this fails, then streptomycin and P.A.S. may be used as a corollary to the present method of using streptomycin and P.A.S. first, then isoniazid.

The signal absence of toxicity of the isoniazid drugs, their undoubted antituberculosis action and the ease with which they are administered orally makes one sanguine enough to hope that these drugs may prove to be a real advance in the chemotherapy of tuberculosis.

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SPECIAL SECTIONS

TRENDS

BY JOHN P. HUBBARD, M.D., *Contributing Editor*

Statements appearing in this column do not necessarily reflect the opinion of the editor nor are they to be interpreted as the official opinion of the Academy.

PROGRAM OF THE COMMITTEE ON CHILD HEALTH OF THE AMERICAN PUBLIC HEALTH ASSOCIATION

A statement prepared by Dr. Samuel M. Wishik, Chairman

THE Committee on Child Health of the American Public Health Association has undertaken the preparation of guides on various types of child health programs. Written primarily for the public health worker, these guides should also prove of interest to the pediatrician in private practice. The statements are being prepared by different organizations and individuals and are at the present time in varying stages of development.

There follows a list of the materials now in preparation and some of the persons helping to draft and design the statements:

Health Supervision of the Well Young Child With Special Reference to the Child Health Conference—Committee on Child Health.

Heart Disease and Rheumatic Fever—American Heart Association.

Visual Defects—National Society for the Prevention of Blindness.

Emotional Disturbances—a committee headed by Jules V. Coleman, M.D.

Orthopedic and Chronic Neurologic Defects (except Cerebral Palsy)—a committee headed by Louis Spekter, M.D.

Diabetes—a committee headed by Hugh L. C. Wilkerson, M.D.

Orthodontic Handicaps—Henry C. Sandler, D.M.D., and the American Association of Orthodontists.

Epilepsy—Harriot Hunter, M.D.

Impaired Hearing—Committee on Child Health.

Cleft Palate and Cleft Lip—Committee on Child Health and the American Association for Cleft Palate Rehabilitation.

Cerebral Palsy—Committee on Child Health and the American Academy for Cerebral Palsy.

General Statement of Principles on the Care of Handicapped Children, Regardless of Diagnosis—Committee on Child Health.

The scope and content of the statements can be discerned by the general outline which they will more or less follow.

I. Introduction
   A. Definition of Handicap
   B. Background, History and Current Status
   C. Determination of Need for Program
   D. Administration of Program
II. Causes of the Handicap
III. Prevention of the Handicap
IV. Case Finding
   Register and reporting
V. Special Diagnosis and Consultation
   A. Diagnostic Aids
   B. Diagnostic Criteria
   C. Consultative Services
VI. Standards of Care
   A. Program planning for
      1. Medical and surgical care
      2. Social, psychological, recreational care
      3. Educational and vocational opportunities
   B. Locations for care
      1. Private homes
      2. Office and hospital out-patient
      3. Hospital in-patient
      4. Schools
      5. Foster homes
      6. Institutions
   C. Follow-up Care and Continuity of Supervision
VII. Professional Personnel Involved in Care of Handicapped Individual
   A. Type
   B. Qualifications
   C. Professional Education (undergraduate, and post-graduate, including in-service training)
VIII. Non-Professional Personnel Involved in Care of Handicapped Individual
   A. Parents
   B. Volunteers
IX. Community Participation
   A. Community education
   B. Participating groups and agencies
X. Program Study
   A. Periodic Evaluation
   B. Public Health Research
IX. Budgets
   Source of funds

The Committee on Child Health consists of 16 members representing physicians, nurses, dentists, nutritionists, educators and other professional persons working with children. A number of the physicians on the Committee are also members of the American Academy of Pediatrics. The Committee is under the Chairmanship of Samuel M. Wishik, M.D., Professor of Maternal and Child Health at the Graduate School of Public Health of the University of Pittsburgh. In addition to the Committee members, more than 60 outstanding national authorities act on subcommittees in the preparation of the several statements. Early drafts of the statements are circulated throughout the country and have already had the active participation of more than a thousand persons in their criticism and change.

Close liaison is being maintained with the American Academy of Pediatrics' Committee on Mentally and Physically Handicapped Children under the Chairmanship of Dr. George F. Munns, through having a number of members in common on both committees and through circulation of early drafts of the statements.

It is likely that there will be joint sponsorship of publication of a number of the statements by various organizations in addition to the American Public Health Association. It is hoped that the American Academy of Pediatrics may become a sponsoring group for some or all of the guides.

NEWS AND ANNOUNCEMENTS

"Adolescence" will be the theme of this year's intensive postgraduate refresher course for pediatricians, Feb. 23 through 27 inclusive at Tulane Medical School. Dr. Joseph A. Johnston of the Henry Ford Hospital will serve as guest lecturer; a full program has been arranged, covering nutritional, endocrinologic, psychiatric, gynecologic, orthopedic, dental, dermatologic and general medical problems. Those interested may secure full information and application forms by addressing the Director, Division of Graduate Medicine, 1430 Tulane Avenue, New Orleans.

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An intensive course on Practical Aspects of Common Endocrine and Metabolic Disorders of Children and Adolescents will be given under the auspices of the Harvard Medical School at the Massachusetts General Hospital on April 16-18, 1953, which are the 3 days immediately preceding the Boston meeting of the American Academy of Pediatrics. Those interested should write to the Assistant Dean, Courses for Graduates, Harvard Medical School, Boston 15. Attendance will be limited.

BOOK REVIEW

HANDBOOK OF PEDIATRIC MEDICAL EMERGENCIES, Adolph G. DeSanctis, M.D., and Charles Varga, M.D., St. Louis, C. V. Mosby Company, 1951, $5.00, 284 pp.

This concise handbook is an enlargement of a therapeutic manual used for resident and postgraduate pediatric training. It is deliberately oriented to immediate treatment with only brief diagnostic criteria included.

Any acute illness of infants or children is rightly considered a pediatric emergency by the authors. There are sections on cardiovascular, genitourinary, gastrointestinal (including dehydration therapy), neurologic, respiratory, poisoning, and premature emergencies. The section on poisoning is particularly noteworthy. Specific antidotes, general therapy and a comprehensive list of common sources of poisons are given.

An illustrated section of pediatric procedures shows the feasibility of practicing the precise therapy outlined.

This is an excellent book for any physician who treats children.